** Paul Schulwitz please - Please return all attachments with search results. Thanks LMD

Access DB# 100995

SEARCH REQUEST FORM

RECEIVED
AUG 12 2003

Scientific and Technical Information Center

(STIC)

Requester's Full Name: MOLLY CEPERLEY Examiner #: 59757 Date: 8/12/03
Art Unit: 1641 Phone Number 30 8-4234 Serial Number: 10/670,302
Mail Box and Bldg/Room Location: 8D15 Results Format Preferred (circle): PAPER (DISK) E-MAIL
↳ 7E12

If more than one search is submitted, please prioritize searches in order of need.

****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: _____

Inventors (please provide full names): _____ See bibliographic data sheet attached.

_____

Earliest Priority Filing Date: _____

***For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.**

Please search for the compound of formula (I) of claim 1 in combination with the terms: ANTIBODY, IMMUNOGEN, HAPTEN, BOVINE SERUM ALBUMIN (BSA), OVALBUMIN (OVA), HORSERADISH PEROXIDASE (HRP), ANTIGEN, IMMUNOASSAY, ELISA (Enzyme linked immunosorbent assay).

The compounds of formula (I) are CYANOBACTERIAL HEPATOTOXINS (e.g. MICROCYSTIN and NODULARIN congeners) which come from M. aeruginosa (microcystis?) and Nodularia.

(*) I am basically looking for the antibodies which react with formula (I)

****

STAFF USE ONLY	Type of Search		Vendors and cost where applicable	
Searcher:	NA Sequence (#)		STN	677 80
Searcher Phone #:	AA Sequence (#)		Dialog	
Searcher Location:	Structure (#)	3	Questel/Orbit	
Date Searcher Picked Up:	8/13	Bibliographic	Dr.Link	
Date Completed:	8/13	Litigation	Lexis/Nexis	
Searcher Prep & Review Time:	15	Fulltext	Sequence Systems	
Clerical Prep Time:		Patent Family	WWW/Internet	
Online Time:	25	Other	Other (specify)	

PTO-1590 (8-01)

WEST Search History

10/070,302

DATE: Wednesday, August 13, 2003

Set Name side by side	Query	Hit Count	Set Name result set
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L7	L6 same l4	1	L7
L6	antibody or antibodies or immuno$ or antigen$	89441	L6
L5	L4 same (l3 or l2 or l1)	4	L5
L4	ADDA	178	L4
L3	nodularia	15	L3
L2	microcystin or nodularin	61	L2
L1	cyanobacterium or cyanobacteria	794	L1

END OF SEARCH HISTORY

Considered 08/15/03 ME

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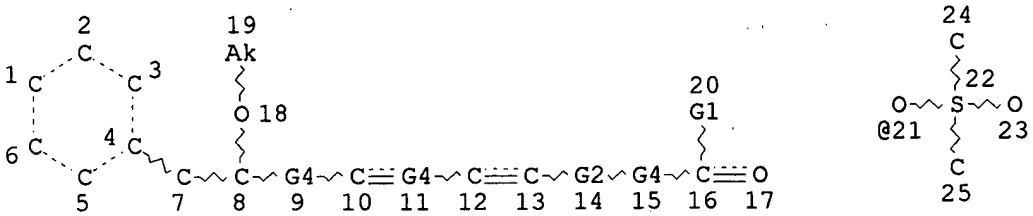

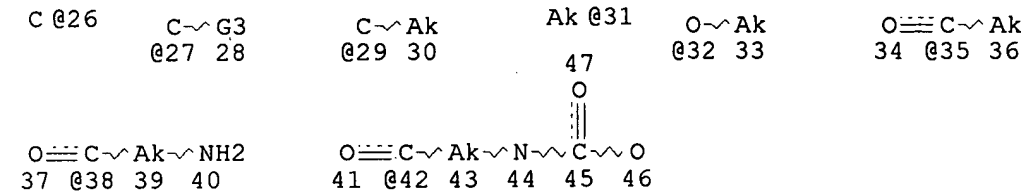

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DEFAULT ECLEVEL IS LIMITED

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NUMBER OF NODES IS 47

STEREO ATTRIBUTES: NONE
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10/070,202

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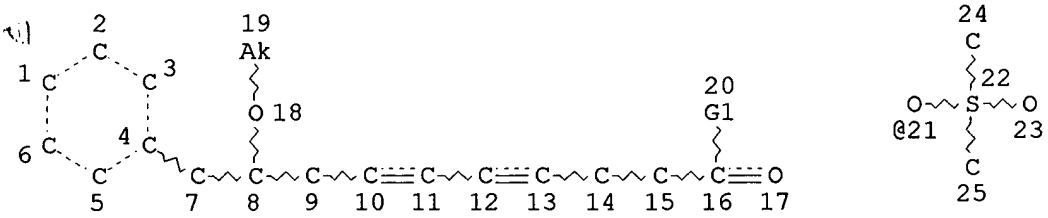

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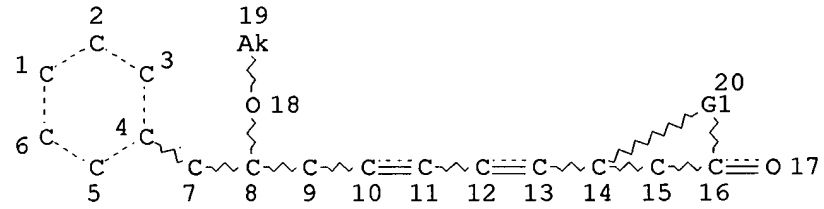

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DEFAULT ECLEVEL IS LIMITED

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STEREO ATTRIBUTES: NONE
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L10           43 SEA FILE=REGISTRY ABB=ON  PLU=ON  L6 OR L9
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L12           33 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L11 AND (ANTIBOD? OR IMMUNO?
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=> d ibib abs hitstr l12 1-33

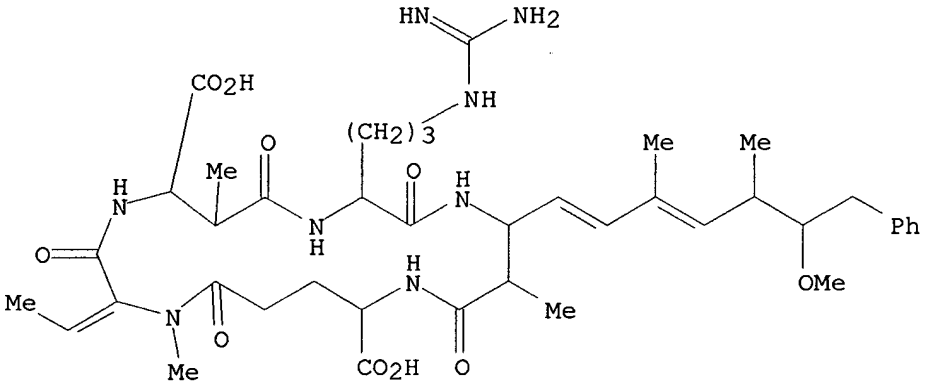
L12  ANSWER 1 OF 33  HCAPLUS  COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER:         2003:120321  HCAPLUS
DOCUMENT NUMBER:          138:132287
```

TITLE: Analysis of Cyanobacterial Toxins by **Immunological** Methods
AUTHOR(S): Metcalf, J. S.; Codd, G. A.
CORPORATE SOURCE: Division of Environmental and Applied Biology School of Life Sciences, University of Dundee, Dundee, DD1 4HN, UK
SOURCE: Chemical Research in Toxicology (2003), 16(2), 103-112
CODEN: CRTOEC; ISSN: 0893-228X
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review on prodn. of antibodies against cyanobacterial toxins (saxitoxins, microcystins and nodularins), applications of microcystin **antibodies** for the anal. of cyanobacterial toxins in water, for investigations of microcystins and nodularins in cyanobacterial cells and in exposed human, animal, and plant materials, methodol. constraints and requirements, and **antibodies**, aptamers, and molecularly imprinted polymers.

IT **118399-22-7**, Nodularin
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(cyanobacterial toxins analyzed by **immunol.** methods)

RN 118399-22-7 HCAPLUS
CN Cyclo[L-arginyl-(2S,3S,4E,6E,8S,9S)-3-amino-9-methoxy-2,6,8-trimethyl-10-phenyl-4,6-decadienoyl-D-.gamma.-glutamyl-(2Z)-2-(methylamino)-2-butenoyl-(3S)-3-methyl-D-.beta.-aspartyl] (9CI) (CA INDEX NAME)



REFERENCE COUNT: 91 THERE ARE 91 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

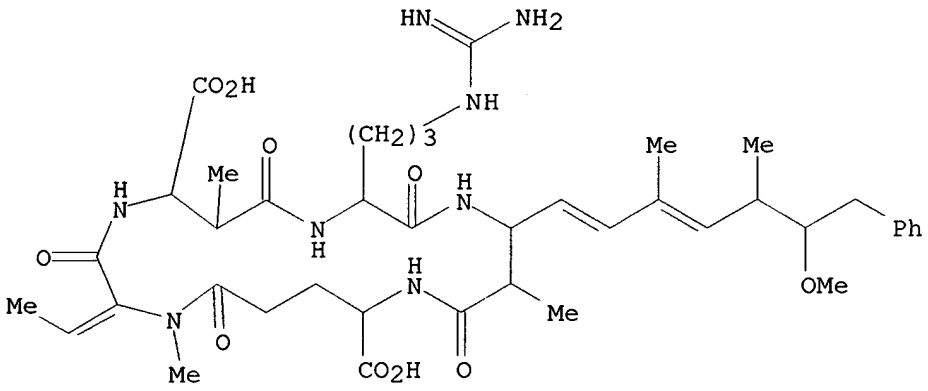
L12 ANSWER 2 OF 33 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:118930 HCAPLUS
DOCUMENT NUMBER: 139:64527
TITLE: Mass spectrometric detection of nodularin and desmethylnodularin in mussels and flounders
AUTHOR(S): Karlsson, Krister; Sipia, Vesa; Kankaanpaa, Harri; Meriluoto, Jussi
CORPORATE SOURCE: Department of Biochemistry and Pharmacy, Abo Akademi University, Turku, 20521, Finland
SOURCE: Journal of Chromatography, B: Analytical Technologies

in the Biomedical and Life Sciences (2003), 784(2), 243-253.
CODEN: JCBAAI; ISSN: 1570-0232
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Samples of mussels and flounders from the Baltic Sea were analyzed for nodularin content on two different LC-MS instruments (triple quadrupole and ion trap). The triple quadrupole instrument was well suited for the quant. anal. The limit of detection in the selected ion recording mode was 5 pg and in the multiple reactant monitoring mode 500 pg on column for exts. of Nodularia spumigena. The fragmentation patterns of nodularin-R and desmethylnodularin-R were recorded and shown to be similar to those of microcystins. LC-MS proved to be an excellent tool for the analyses of cyanobacterial hepatotoxins in complex matrixes.

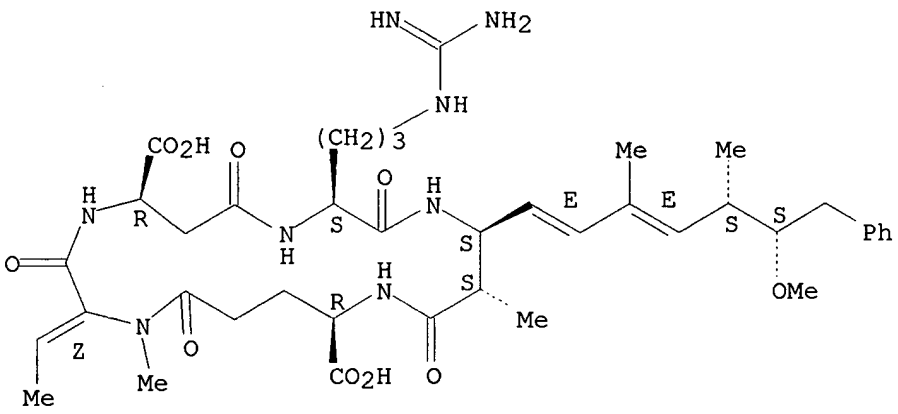
IT **118399-22-7,** Nodularin-R **159410-68-1**
RL: ANT (Analyte); ANST (Analytical study)
(mass spectrometric detection of nodularin and desmethylnodularin in mussels and flounders)

RN 118399-22-7 HCAPLUS
CN Cyclo[L-arginyl-(2S,3S,4E,6E,8S,9S)-3-amino-9-methoxy-2,6,8-trimethyl-10-phenyl-4,6-decadienoyl-D-.gamma.-glutamyl-(2Z)-2-(methylamino)-2-butenoyl-(3S)-3-methyl-D-.beta.-aspartyl] (9CI) (CA INDEX NAME)



RN 159410-68-1 HCAPLUS
CN Cyclo[L-arginyl-(2S,3S,4E,6E,8S,9S)-3-amino-9-methoxy-2,6,8-trimethyl-10-phenyl-4,6-decadienoyl-D-.gamma.-glutamyl-(2Z)-2-(methylamino)-2-butenoyl-D-.beta.-aspartyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 3 OF 33 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:947234 HCAPLUS
DOCUMENT NUMBER: 138:102242
TITLE: Bioaccumulation and detoxication of nodularin in tissues of flounder (Platichthys flesus), mussels (Mytilus edulis, Dreissena polymorpha), and clams (Macoma balthica) from the northern Baltic Sea
AUTHOR(S): Sipia, V. O.; Kankaanpaa, H. T.; Pflugmacher, S.; Flinkman, J.; Furey, A.; James, K. J.
CORPORATE SOURCE: Finnish Institute of Marine Research, Helsinki, FIN-00931, Finland
SOURCE: Ecotoxicology and Environmental Safety (2002), 53(2), 305-311
CODEN: EESADV; ISSN: 0147-6513
PUBLISHER: Elsevier Science
DOCUMENT TYPE: Journal
LANGUAGE: English

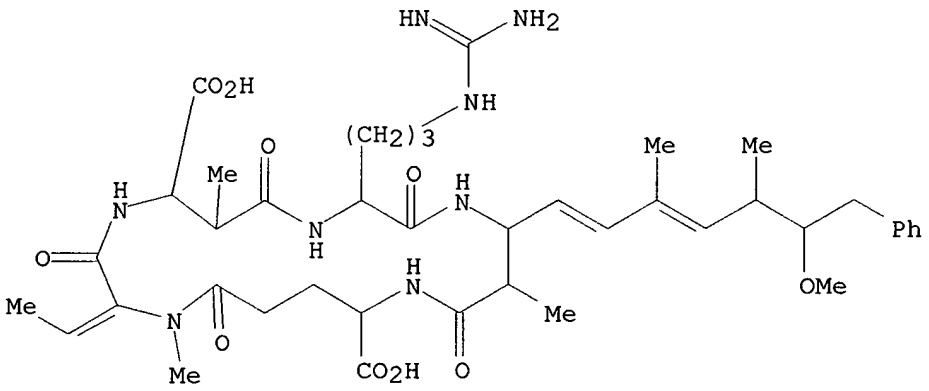
AB Cyanobacterial hepatotoxin accumulation in mussels (Mytilus edulis, Dreissena polymorpha), clam (Macoma balthica), and flounder (Platichthys flesus) tissues was measured. Flounder were caught with gillnets from the western Gulf of Finland on 21 August 1999, 25 July 2000, and 25 August 2000. Blue mussels were collected from: (1) a steel cage at a depth of 3 m on 20 August 1999, (2) an enclosure at depths of 3-5 m, and (3) an artificial reef (wreck at 25-30 m) in the western Gulf of Finland between June and Sept. 2000. Furthermore, blue mussels were collected from two sites between August and Oct. 2000: south of the town of Hanko at depths of 5 and 20 m in the western Gulf of Finland and south of the city of Helsinki at a depth of 7 m in the central Gulf of Finland. M. balthica and D. polymorpha were collected at a depth of 12 m from Russian waters in the eastern Gulf of Finland on 1-4 August 2000. The samples were analyzed for the cyanobacterial hepatotoxins nodularin (NODLN) and microcystins (MCs) using **ELISA** (**ELISA**), liq. chromatog.-mass spectrometry (LC-MS), and matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF-MS). **ELISA** indicated a time-dependent accumulation of hepatotoxins in flounder liver up to 400 .+-. 10 (SD) .mu.g/kg on 25 August 2000. No hepatotoxins were detected in flounder muscle samples. In blue mussels, collected from an enclosure 3-5 m deep in the western Gulf of Finland on 23 August 2000,

ELISA indicated cyanobacterial hepatotoxins up to 1490 .+-. 60 .mu.g/kg dry wt. Blue mussels collected from the other sites contained less cyanobacterial hepatotoxins (40-130 .mu.g/kg dry wt). Clams and mussels from Russian waters contained cyanobacterial hepatotoxin at about 100-130 .mu.g/kg dry wt. Total hepatotoxin levels in mussels from enclosures decreased from August to Sept., indicating at least partial detoxication/depuration of the toxins. LC-MS verified the presence of NODLN in mussels and flounder. Typical detoxication conjugates were obsd. by MALDI-TOF-MS in mussel samples collected during August 2000. In deeper-living wreck mussels cyanobacterial hepatotoxin levels continued to increase, from August to Sept., indicating that portions of cyanobacterial hepatotoxins reach the sea floor. NODLN bioaccumulation is a const. phenomenon in the area.

IT **118399-22-7**, Nodularin
RL: PKT (Pharmacokinetics); POL (Pollutant); BIOL (Biological study); OCCU (Occurrence)
(hepatotoxin nodularin accumulation and detoxification in mussels, clam, and flounder tissue)

RN 118399-22-7 HCAPLUS

CN Cyclo[L-arginyl-(2S,3S,4E,6E,8S,9S)-3-amino-9-methoxy-2,6,8-trimethyl-10-phenyl-4,6-decadienoyl-D-.gamma.-glutamyl-(2Z)-2-(methylamino)-2-butenoyl-(3S)-3-methyl-D-.beta.-aspartyl] (9CI) (CA INDEX NAME)



REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 4 OF 33 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2002:784996 HCAPLUS
DOCUMENT NUMBER: 137:347736
TITLE: Does cyanobacterial toxin accumulate in mysid shrimps and fish via copepods?
AUTHOR(S): Engstrom-Ost, Jonna; Lehtiniemi, Maiju; Green, Sandra; Kozlowsky-Suzuki, Betina; Viitasalo, Markku
CORPORATE SOURCE: Finnish Institute of Marine Research, Helsinki, FIN-00931, Finland
SOURCE: Journal of Experimental Marine Biology and Ecology (2002), 276(1-2), 95-107
CODEN: JEMBAM; ISSN: 0022-0981
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal

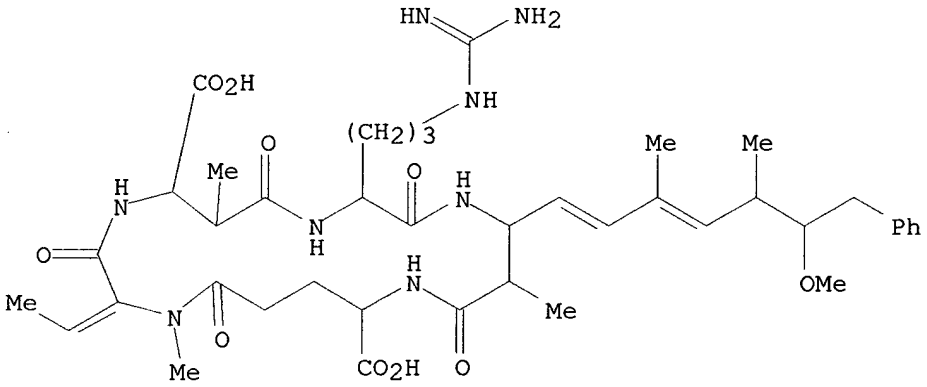
LANGUAGE: English

AB It has been suggested that pelagic planktivores may receive cyanobacterial toxins indirectly, i.e., by preying on organisms that have ingested cyanobacteria. The authors tested this hypothesis in lab. conditions by providing mysid shrimps, Mysis relicta, and three-spined sticklebacks, Gasterosteus aculeatus, with cyanobacteria-fed copepods. The aim of the study was to observe the potential transfer and accumulation of the toxin nodularin, produced by the cyanobacteria Nodularia spumigena, in planktivore tissue during the 10-day trials. The concn. of nodularin was measured by 2 toxin detection methods, **ELISA** and protein phosphatase (PPase) inhibition assay. The **ELISA** results showed that the toxin concns. in mysid tissue were significantly higher than in fish tissue, whereas no differences between species were detected by the PPase inhibition assay. The concns. measured by **ELISA** suggested that accumulation had taken place in mysids, since the toxin increased with time in the animals. The concns., measured by PPase inhibition assay, were significantly higher than the ones measured by **ELISA** . Thus, the cyanobacterial toxin may accumulate in higher trophic levels via copepods and the results are more reliable if analyzed with several methods.

IT **118399-22-7**, Nodularin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(cyanobacterial toxin accumulation in mysid shrimps and fish via copepods)

RN 118399-22-7 HCAPLUS

CN Cyclo[L-arginyl-(2S,3S,4E,6E,8S,9S)-3-amino-9-methoxy-2,6,8-trimethyl-10-phenyl-4,6-decadienoyl-D-.gamma.-glutamyl-(2Z)-2-(methylamino)-2-butenoyl-(3S)-3-methyl-D-.beta.-aspartyl] (9CI) (CA INDEX NAME)



REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 5 OF 33 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:740062 HCAPLUS
DOCUMENT NUMBER: 138:51205
TITLE: Acute effects and bioaccumulation of nodularin in sea trout (Salmo trutta m. trutta L.) exposed orally to Nodularia spumigena under laboratory conditions
AUTHOR(S): Kankaanpaa, Harri; Vuorinen, Pekka J.; Sipia, Vesa; Keinanen, Marja

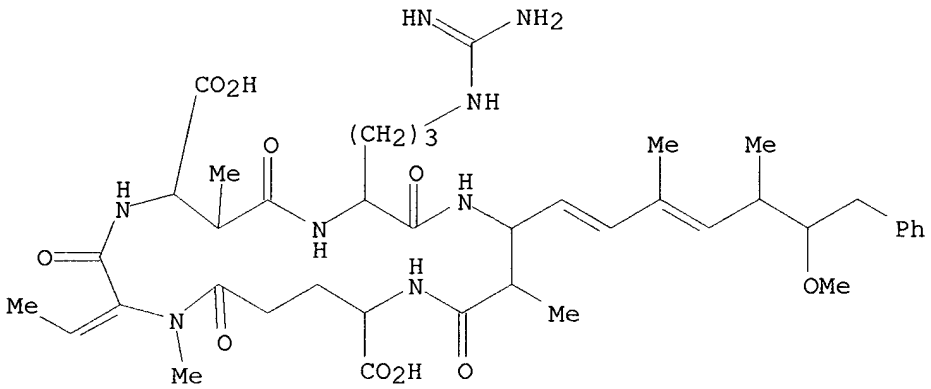
CORPORATE SOURCE: Finnish Institute of Marine Research, Helsinki, FIN-00931, Finland
SOURCE: Aquatic Toxicology (2002), 61(3-4), 155-168
CODEN: AQTODG; ISSN: 0166-445X
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

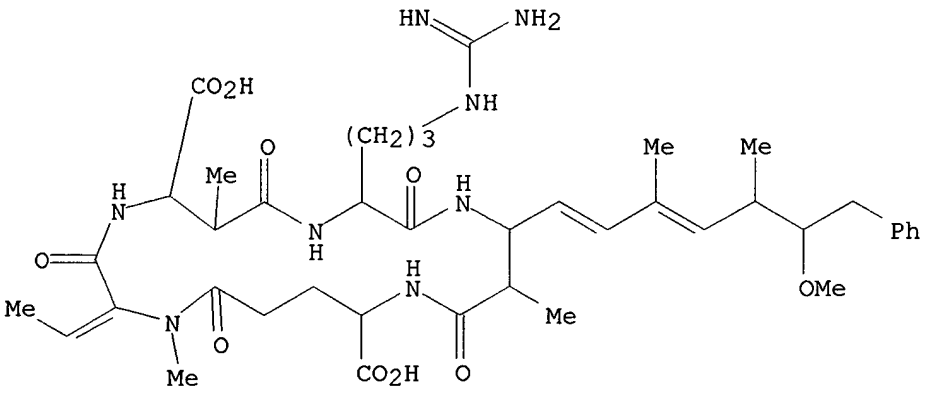
AB Nodularin (NODLN) is a cyclic pentapeptide hepatotoxin that is regularly produced in high amts. by the cyanobacterium Nodularia spumigena in the Baltic Sea, and can bioaccumulate in Baltic biota. Baltic sea trout (Salmo trutta m. trutta L.) were exposed orally to a single dose of food contg. NODLN (125 mg/kg ww) from N. spumigena (strain AV1, from the Baltic Sea). The level of exposure was 210-620 (av. 440) .mu.g NODLN per kg bw. Based on an 8-day survey under lab. conditions, NODLN-like compds. accumulated in trout liver, with increasing liver concns. (from 19 .mu.g/kg on day 1 up to 1200 .mu.g/kg on day 8 as measured with the EnviroLogix ELISA kit). during the expt. Thus, accumulation of NODLN-like compds. in liver increased from 0.05% of the total NODLN dose administered on day 1 to 0.53% on day 8. However, the **ELISA** test kit is also sensitive to metabolites of algal hepatotoxins. In the HPLC chromatograms, no NODLN peak was detected after 24 h that also suggested NODLN absorbed in trout was metabolized or bound rapidly. According to **ELISA**, NODLN-like compds. also accumulated in trout muscle in lower quantities (from 125 to 34 .mu.g/kg dw). Histopathol. revealed complete loss of liver architecture after 1-2 days of the single oral dose. From day 4 to 8, there was partial recovery of liver cells. NODLN did not affect thiamin levels or water content of trout liver. The results showed that NODLN rapidly induces severe but reversible liver damage. Apparently NODLN accumulated in trout liver from cyanobacteria in the intestine, but was detoxified rapidly. On the basis of discrepancies between the histopathol. and **ELISA**, and on the other hand, between the HPLC and **ELISA** methods, anal. of NODLN and its metabolites in biol. tissue needs to be improved.

IT **118399-22-7**, Nodularin
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(acute effects and bioaccumulation of nodularin in sea trout (Salmo trutta) exposed orally to Nodularia spumigena under lab. conditions)

RN 118399-22-7 HCAPLUS

CN Cyclo[L-arginyl-(2S,3S,4E,6E,8S,9S)-3-amino-9-methoxy-2,6,8-trimethyl-10-phenyl-4,6-decadienoyl-D-.gamma.-glutamyl-(2Z)-2-(methylamino)-2-butenoyl-(3S)-3-methyl-D-.beta.-aspartyl] (9CI) (CA INDEX NAME)





REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 6 OF 33 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:452065 HCAPLUS
DOCUMENT NUMBER: 137:78111
TITLE: Development of a Sensitive **ELISA** for the Determination of Microcystins in Algae
AUTHOR(S): Yu, Feng-Yih; Liu, Biing-Hui; Chou, Hong-Nong; Chu, Fun Sun
CORPORATE SOURCE: Department of Life Science, Chung Shan Medical University, Taichung, Taiwan
SOURCE: Journal of Agricultural and Food Chemistry (2002), 50(15), 4176-4182
CODEN: JAFCAU; ISSN: 0021-8561
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

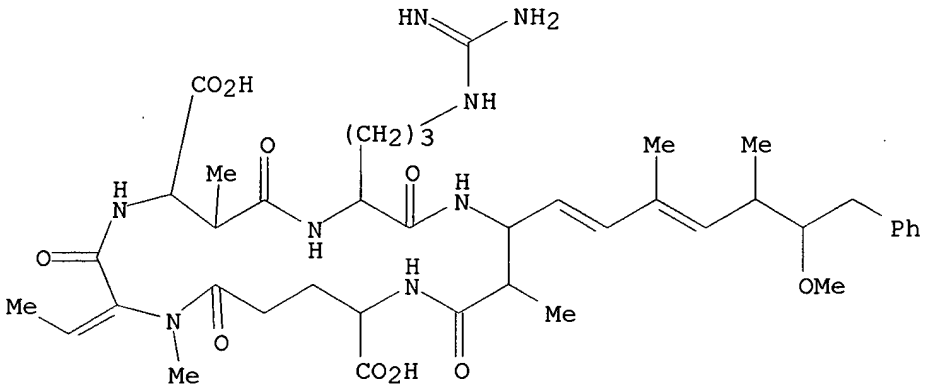
AB Polyclonal **antibodies** for microcystin-leucine-arginine (MCYST-LR) were generated from rabbits after immunizing the animals with MCYST-LR conjugated with .gamma.-globulin. A competitive direct **ELISA** (cdELISA) and a competitive indirect **ELISA** (ciELISA) were used for the characterization of the **antibodies** and for anal. of the toxin in algal cultures and dietary supplements. The concns. causing 50% inhibition (IC50) of binding of MCYST-horseradish peroxidase (MCYST-HRP) to the solid-phase **antibodies** by MCYST-LR, MCYST-arginine-arginine variant (MCYST-RR), MCYST-tyrosine-arginine variant (MCYST-YR), and nodularin (NODLN) in the cdELISA were found to be 0.10, 0.12, 0.14, and 0.20 ng/mL, resp. In the presence of algae matrix, the detection limit is less than 10 ppb. The overall anal. recovery of MCYST-LR (25 to 500 ng/g) added to the algal dietary supplements and then extd. with 0.1 M ammonium bicarbonate in the cdELISA was found to be 83.7%. Anal. of MCYSTs in algal cultures and dietary supplements showed that six of eleven cultures produce MCYSTs, and five of the algal cultures were not MCYST producers. Eight of eleven tested com. algal dietary supplements contained MCYSTs at a level lower than 100 ppb. The presence of MCYST-LR in the Microcystis aeruginosa culture was confirmed by high-performance liq. chromatog.

IT **118399-22-7,** Nodularin
RL: ANT (Analyte); POL (Pollutant); ANST (Analytical study); OCCU (Occurrence)

(sensitive **ELISA** for detn. of microcystins in algal cultures and dietary supplements)

RN 118399-22-7 HCAPLUS

CN Cyclo[L-arginyl-(2S,3S,4E,6E,8S,9S)-3-amino-9-methoxy-2,6,8-trimethyl-10-phenyl-4,6-decadienoyl-D-.gamma.-glutamyl-(2Z)-2-(methylamino)-2-butenoyl-(3S)-3-methyl-D-.beta.-aspartyl] (9CI) (CA INDEX NAME)



REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 7 OF 33 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2002:194746 HCAPLUS

DOCUMENT NUMBER: 136:275993

TITLE: Toxic cyanobacteria in New Zealand lakes and toxicity to indigenous zooplankton

AUTHOR(S): Christoffersen, Kirsten; Burns, Carolyn W.

CORPORATE SOURCE: Freshwater Biological Laboratory, University of Copenhagen, Hillerod, DK-3400, Den.

SOURCE: Verhandlungen - Internationale Vereinigung fuer Theoretische und Angewandte Limnologie (2001), Volume Date 2000, 27(5), 3222-3225
CODEN: IVTLAP; ISSN: 0368-0770

PUBLISHER: E. Schweizerbart'sche Verlagsbuchhandlung

DOCUMENT TYPE: Journal

LANGUAGE: English

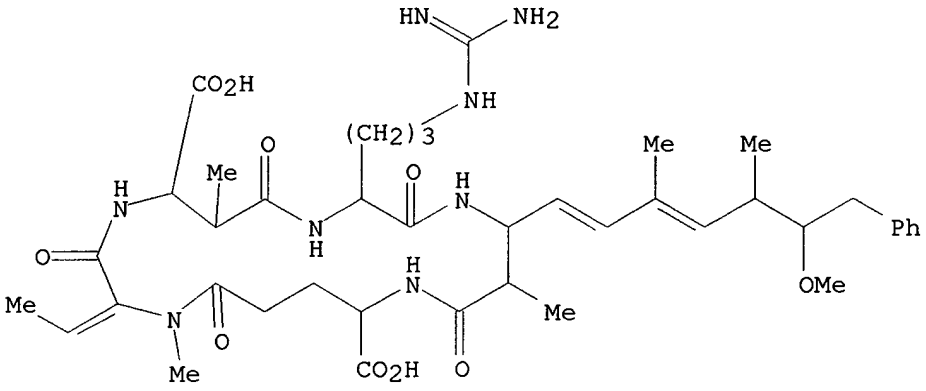
AB Several South Island lakes in New Zealand, in which cyanobacterial blooms had previously been reported, were surveyed to test for the presence of toxins (microcystin and nodularin) and to det. the sensitivity of indigenous zooplankton to microcystin. Toxins were detected in the algal material from six New Zealand lakes during Jan. and Feb. 1996, with toxin concns. ranging between 0.03 and 37.68 .mu.g microcystin equiv. g/FDW. The toxic materials were related to the presence of Anabaena and Microcystis, except in Lake Ellesmere where only a few cyanobacterial cells were found in the fixed algal material. The most toxic lake was Lake Ellesmere while Butchers Dam, Lake Jhonson, and Lake Roundabout were the least toxic. The toxic algal may occur in New Zealand lakes which have cyanobacteria, and the toxicity of dissolved toxins is similar to that of blooms found elsewhere. However, the relatively low algal biomass in most New Zealand lakes makes it unlikely that major toxic effects to humans and livestock will occur provided the magnitude and duration of

cyanobacterial growth does not increase. Algal materials from three lakes contained toxic substances that were not detected by the **ELISA** and that these toxins affected D. carinata. The dissolved concn. in Lake Ellesmere and Lake Rotorua were therefore potentially toxic to indigenous zooplankton if the blooms collapsed.

IT **118399-22-7**, Nodularin
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(cyanobacteria in New Zealand lakes and their toxicity to indigenous zooplankton)

RN 118399-22-7 HCAPLUS

CN Cyclo[L-arginyl-(2S,3S,4E,6E,8S,9S)-3-amino-9-methoxy-2,6,8-trimethyl-10-phenyl-4,6-decadienoyl-D-.gamma.-glutamyl-(2Z)-2-(methylamino)-2-butenoyl-(3S)-3-methyl-D-.beta.-aspartyl] (9CI) (CA INDEX NAME)



REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 8 OF 33 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2002:37131 HCAPLUS

DOCUMENT NUMBER: 136:123145

TITLE: Algal monitoring on the Ohio River: increased concentrations of cyanobacteria

AUTHOR(S): Westrick, Judy; Oehrle, Stuart; Steinitz-Kannan, Miriam

CORPORATE SOURCE: Northern Kentucky University, Highland Heights, KY, 41099, USA

SOURCE: Proceedings - Annual Conference, American Water Works Association (2001) 1263-1274
CODEN: PWACDO; ISSN: 0360-814X

PUBLISHER: American Water Works Association

DOCUMENT TYPE: Journal; (computer optical disk)

LANGUAGE: English

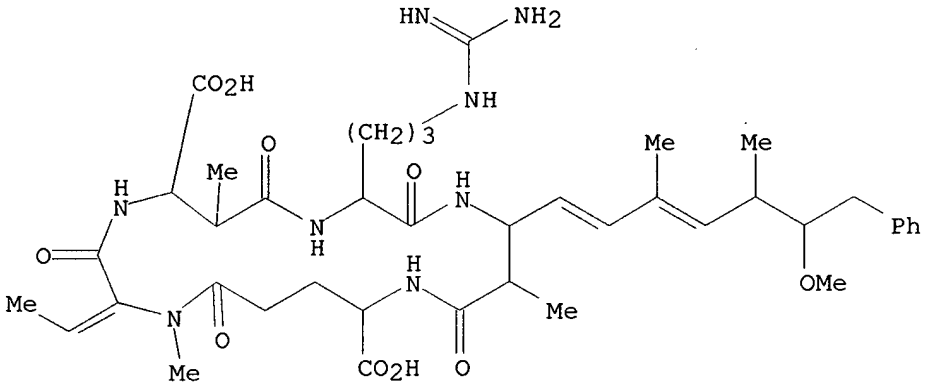
AB The US EPA final Drinking Water Contaminant Candidate List contains fresh water algae including cyanobacteria and their toxins. Current drinking water treatment techniques may be inadequate in controlling pathogenic algae because the current Surface Water Treatment Rule and the Enhanced Surface Water Treatment Rule focus on fecal coliform removal not algae removal. Our research goals are: (1) develop an early algal detection-monitoring program for the drinking water plants on the Ohio

River, (2) evaluate algal removal efficiencies of individual unit processes in conventional treatment drinking water plants, (3) and develop a liq. chromatog./mass spectroscopy (LC/MS) quant. anal. method for the sepn. of microcystin LR, LA, LF, LW, RR,YR and nodularin. Bimonthly algal monitoring (1999-2000) suggests that cyanobacteria blooms occur from Feb. to Nov. in the Ohio River. Aphanizomenon blooms occurred in the early spring, while Microcystis blooms occurred in the late summer/fall months. Many of the river utilities use the Ohio River to recharge storage reservoir waters. These 2 waters have very different algal populations and therefore both sources must be monitored. Through plant monitoring of a conventional water treatment process suggests efficient algae removal. Although this plant experienced several Microcystis blooms, the plant's source waters (Ohio River and storage reservoirs) tested neg. for microcystin by **ELISA** assay and LC/MS. Linear calibration by LC/MS for microcystin LR from 0.125 to 24 ppb was accomplished. Detection of microcystin LR from a cultured sample and spiked river samples using solid phase extn. and LC/MS anal. shows promise for developing a simple, fast, and quant. anal. method.

IT **118399-22-7**, Nodularin
RL: BSU (Biological study, unclassified); POL (Pollutant); BIOL (Biological study); OCCU (Occurrence)
(algal monitoring on Ohio River and increased concns. of cyanobacteria)

RN 118399-22-7 HCAPLUS

CN Cyclo[L-arginyl-(2S,3S,4E,6E,8S,9S)-3-amino-9-methoxy-2,6,8-trimethyl-10-phenyl-4,6-decadienoyl-D-.gamma.-glutamyl-(2Z)-2-(methylamino)-2-butenoyl-(3S)-3-methyl-D-.beta.-aspartyl] (9CI) (CA INDEX NAME)



REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

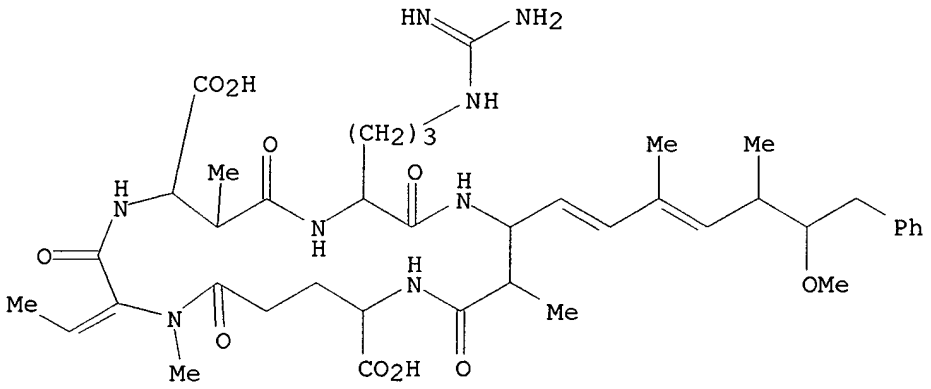
L12 ANSWER 9 OF 33 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:4615 HCAPLUS
DOCUMENT NUMBER: 136:212002
TITLE: Development of a direct competitive microcystin immunoassay of broad specificity
AUTHOR(S): Weller, Michael G.; Zeck, Anne; Eikenberg, Anja; Nagata, Satoshi; Ueno, Yoshio; Niessner, Reinhard
CORPORATE SOURCE: Institute of Hydrochemistry, Technical University of Munich, Munchen, D-81377, Germany
SOURCE: Analytical Sciences (2001), 17(12), 1445-1448

CODEN: ANSCEN; ISSN: 0910-6340
PUBLISHER: Japan Society for Analytical Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The monoclonal **antibody** M8H5 was used in a direct competitive enzyme **immunoassay** performed in microtitration plates. M8H5 **antibody** was produced with a microcystin-LR-**BSA** **immunogen** in BALB/c mice. This **immunoassay** showed a very even cross-reactivity pattern for microcystins and nodularin, suggesting that none of the cross-reactivities (except the non-toxic amino acid Adda) was significantly different from 100%. Thus, the assay is well suited to det. the sum concns. of microcystins in water samples. The detection limit of around 0.05 .mu.g/L is low enough to allow the testing for violations of the proposed WHO level of 1 .mu.g/L for microcystin-LR in drinking water. M8H5 is quite robust against matrix effects, and thus should not be prone to false pos. values.

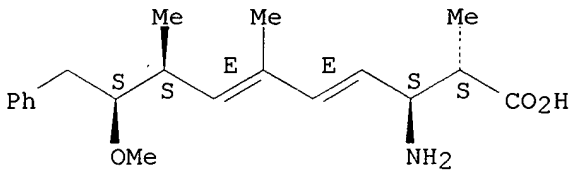
IT **118399-22-7**, Nodularin **126456-06-2**, Adda
RL: ANT (Analyte); ANST (Analytical study)
(development of direct competitive microcystin **immunoassay** of broad specificity for detection in waters)

RN 118399-22-7 HCAPLUS
CN Cyclo[L-arginyl-(2S,3S,4E,6E,8S,9S)-3-amino-9-methoxy-2,6,8-trimethyl-10-phenyl-4,6-decadienoyl-D-.gamma.-glutamyl-(2Z)-2-(methylamino)-2-butenoyl-(3S)-3-methyl-D-.beta.-aspartyl] (9CI) (CA INDEX NAME)



RN 126456-06-2 HCAPLUS
CN 4,6-Decadienoic acid, 3-amino-9-methoxy-2,6,8-trimethyl-10-phenyl-, (2S,3S,4E,6E,8S,9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

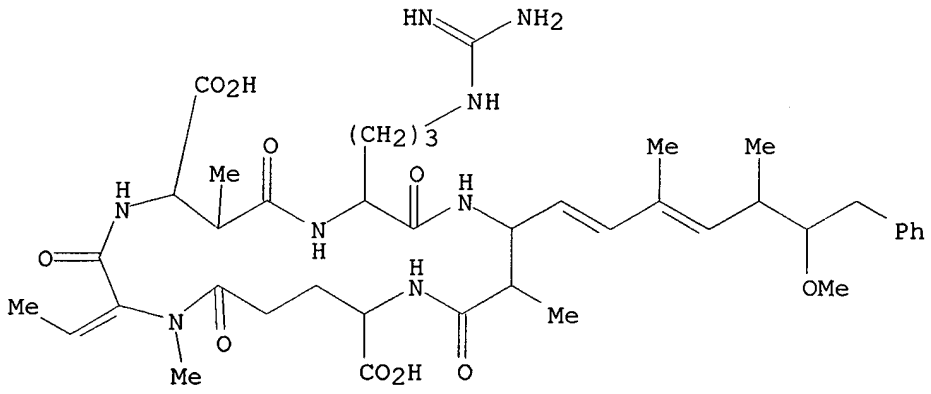
L12 ANSWER 10 OF 33 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:831200 HCAPLUS
DOCUMENT NUMBER: 136:139459
TITLE: Congener-Independent **Immunoassay** for Microcystins and Nodularins
AUTHOR(S): Fischer, Werner J.; Garthwaite, Ian; Miles, Christopher O.; Ross, Kathryn M.; Aggen, James B.; Chamberlin, A. Richard; Towers, Neale R.; Dietrich, Daniel R.
CORPORATE SOURCE: Nestle Research Center, Nestec Ltd., Lausanne, 1000, Switz.
SOURCE: Environmental Science and Technology (2001), 35(24), 4849-4856
CODEN: ESTHAG; ISSN: 0013-936X
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

Inventors

AB Cyanobacteria (blue-green algae) (e.g., Microcystis and Nodularia species) capable of producing toxic peptides are found in fresh and brackish water worldwide. These toxins include the microcystin (MC) heptapeptides (>60 congeners) and the nodularin pentapeptides (.apprx.5 congeners). Cyanobacterial cyclic peptide toxins are harmful to man, other mammals, birds, and fish. Acute exposure to high concns. of these toxins causes liver damage, while subchronic or chronic exposure may promote liver tumor formation. The detection of cyclic peptide cyanobacterial toxins in surface and drinking waters has been hampered by the low limits of detection required and by the fact that the present routine detection is restricted to a few of the congeners. The unusual .beta.-amino acid ADDA (4E,6E-3-amino-9-methoxy-2,6,8-trimethyl-10-phenyldeca-4,6-dienoic acid) is present in most (>80%) of the known toxic penta- and heptapeptide toxin congeners. Here, we report the synthesis of two ADDA-**haptens**, the raising of **antibodies** to ADDA, and the development of a competitive indirect **ELISA** for the detection of microcystins and nodularins utilizing these **antibodies**. The assay has a limit of quantitation of 0.02-0.07 ng/mL (depending on which congeners are present), lower than the WHO-proposed guideline (1 ng/mL) for drinking water, irresp. of the sample matrix (raw water, drinking water, or pure toxin in PBS). This new **ELISA** is robust, can be performed without sample preconcn., detects toxins in freshwater samples at lower concns. than does the protein phosphatase inhibition assay, and shows very good cross-reactivity with all cyanobacterial cyclic peptide toxin congeners tested to date (MC-LR, -RR, -YR, -LW, -LF, 3-desmethyl-MC-LR, 3-desmethyl-MC-RR, and nodularin).

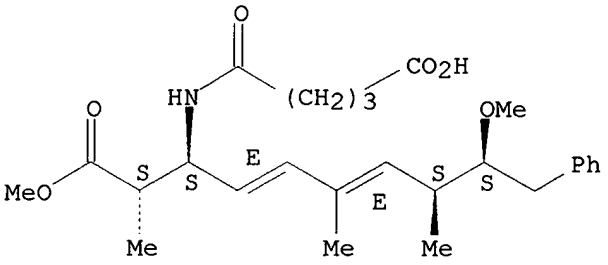
IT **118399-22-7**, Nodularin
RL: ANT (Analyte); ANST (Analytical study)
(congener-independent **immunoassay** for microcystins and nodularin ultratrace detn. in water)

RN 118399-22-7 HCAPLUS
CN Cyclo[L-arginyl-(2S,3S,4E,6E,8S,9S)-3-amino-9-methoxy-2,6,8-trimethyl-10-phenyl-4,6-decadienoyl-D-.gamma.-glutamyl-(2Z)-2-(methylamino)-2-butenoyl-(3S)-3-methyl-D-.beta.-aspartyl] (9CI) (CA INDEX NAME)



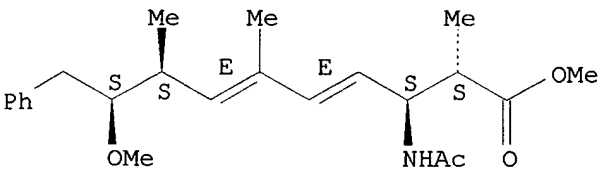
IT **392283-06-6P**
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(**hapten**; prepn. and IR and NMR spectra of and conjugation with albumins for **immunoassay** of microcystins and nodularins)
RN 392283-06-6 HCAPLUS
CN 4,6-Decadienoic acid, 3-[(4-carboxy-1-oxobutyl)amino]-9-methoxy-2,6,8-trimethyl-10-phenyl-, 1-methyl ester, (2S,3S,4E,6E,8S,9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



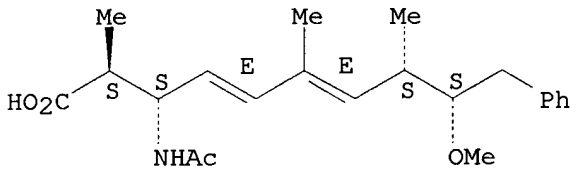
IT **329791-61-9P**
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and IR and NMR spectra and hydrolysis of)
RN 329791-61-9 HCAPLUS
CN 4,6-Decadienoic acid, 3-(acetylamino)-9-methoxy-2,6,8-trimethyl-10-phenyl-, methyl ester, (2S,3S,4E,6E,8S,9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



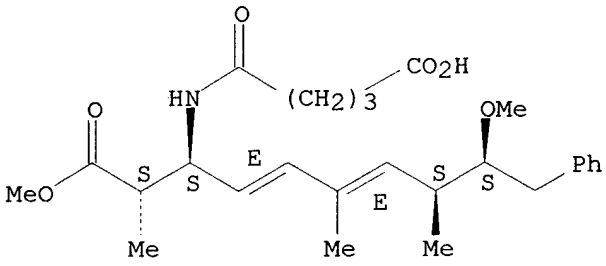
IT **329791-62-0**
RL: PRP (Properties); RCT (Reactant); RACT (Reactant or reagent)
(prepn. and NMR of and reaction with D-alanine Me ester hydrochloride)
RN 329791-62-0 HCAPLUS
CN 4,6-Decadienoic acid, 3-(acetylamino)-9-methoxy-2,6,8-trimethyl-10-phenyl-, (2S,3S,4E,6E,8S,9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



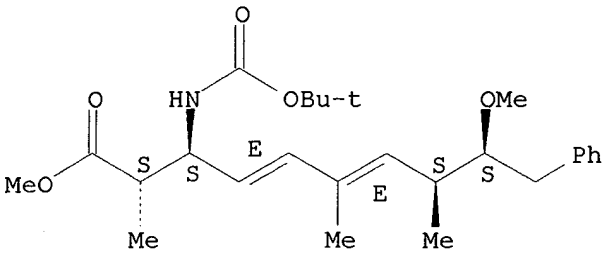
IT **392283-06-6D**, conjugates with **ovalbumin**
RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)
(prepn. and **antibody** induction thereby for **immunoassay** of microcystins and nodularins in water)
RN 392283-06-6 HCAPLUS
CN 4,6-Decadienoic acid, 3-[(4-carboxy-1-oxobutyl)amino]-9-methoxy-2,6,8-trimethyl-10-phenyl-, 1-methyl ester, (2S,3S,4E,6E,8S,9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



IT **134440-91-8**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction with acetic anhydride)
RN 134440-91-8 HCAPLUS
CN 4,6-Decadienoic acid, 3-[[(1,1-dimethylethoxy)carbonyl]amino]-9-methoxy-2,6,8-trimethyl-10-phenyl-, methyl ester, (2S,3S,4E,6E,8S,9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



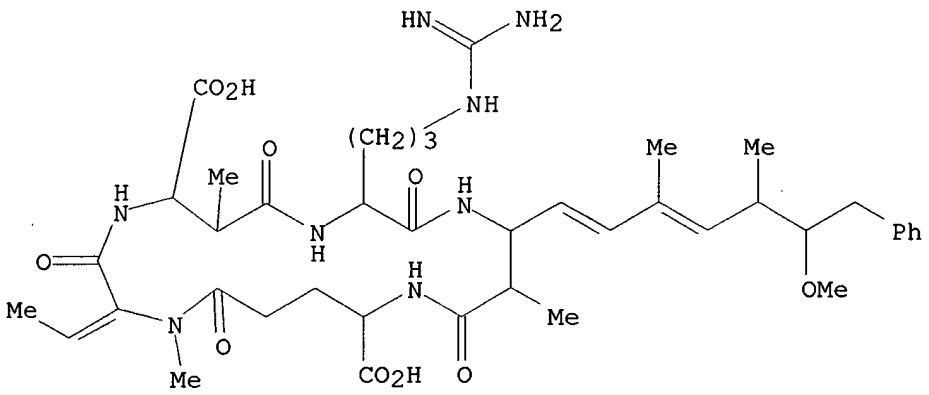
REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 11 OF 33 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:815009 HCAPLUS
DOCUMENT NUMBER: 136:299330
TITLE: Generic microcystin **immunoassay** based on monoclonal **antibodies** against Adda
AUTHOR(S): Zeck, Anne; Weller, Michael G.; Bursill, Don; Niessner, Reinhard
CORPORATE SOURCE: Institute of Hydrochemistry, Technical University of Munich, Munich, 81377, Germany
SOURCE: Analyst (Cambridge, United Kingdom) (2001), 126(11), 2002-2007
CODEN: ANALAO; ISSN: 0003-2654
PUBLISHER: Royal Society of Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A monoclonal **antibody** (clone AD4G2) was generated against a common part of microcystins and nodularins, the unusual amino acid Adda. A direct competitive **ELISA** based on this **antibody** was developed and the cross-reactivity pattern was measured. Different toxins showed a very similar response. The assay provides therefore a sum parameter of microcystins, nodularins and peptide fragments contg. Adda. The IC50 for microcystin-LR was 0.33 .mu.g/L which leads to a detection limit of 0.07 .mu.g/L. This is well below the concn. of 1 .mu.g/L proposed by the WHO as the limit for drinking water. Microcystin-LR spiked water samples at concns. 0.1-1 .mu.g/L were measured with a mean recovery of 113.+-.23%. The **antibody** is well suited for the detn. of microcystins in drinking and surface waters.

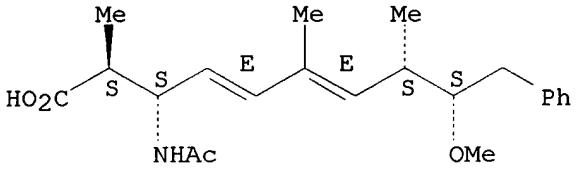
IT **118399-22-7**, Nodularin-R **329791-62-0**
RL: ANT (Analyte); ANST (Analytical study)
(generic microcystin **immunoassay** based on monoclonal **antibodies** against Adda)

RN 118399-22-7 HCAPLUS
CN Cyclo[L-arginyl-(2S,3S,4E,6E,8S,9S)-3-amino-9-methoxy-2,6,8-trimethyl-10-phenyl-4,6-decadienoyl-D-.gamma.-glutamyl-(2Z)-2-(methylamino)-2-butenoyl-(3S)-3-methyl-D-.beta.-aspartyl] (9CI) (CA INDEX NAME)



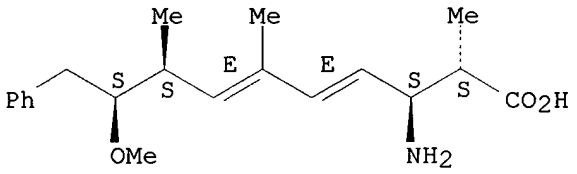
RN 329791-62-0 HCAPLUS
CN 4,6-Decadienoic acid, 3-(acetylamino)-9-methoxy-2,6,8-trimethyl-10-phenyl-, (2S,3S,4E,6E,8S,9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



IT **126456-06-2**, Adda
RL: ANT (Analyte); ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(generic microcystin **immunoassay** based on monoclonal **antibodies** against Adda)
RN 126456-06-2 HCAPLUS
CN 4,6-Decadienoic acid, 3-amino-9-methoxy-2,6,8-trimethyl-10-phenyl-, (2S,3S,4E,6E,8S,9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 12 OF 33 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:761137 HCAPLUS
DOCUMENT NUMBER: 136:291595

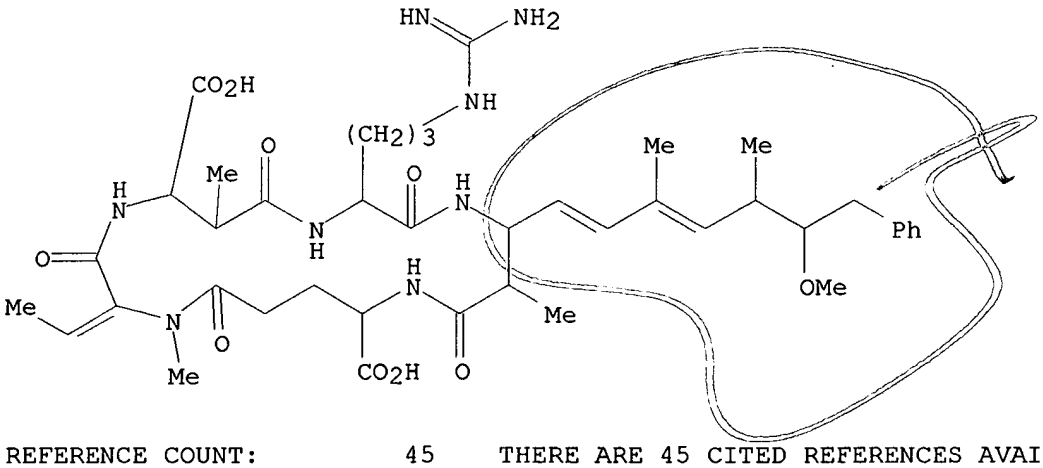
TITLE: Diversity of toxic and nontoxic Nodularia isolates (cyanobacteria) and filaments from the Baltic Sea
AUTHOR(S): Laamanen, Maria J.; Gugger, Muriel F.; Lehtimaki, Jaana M.; Haukka, Kaisa; Sivonen, Kaarina
CORPORATE SOURCE: Department of Applied Chemistry and Microbiology, University of Helsinki, 00014, Finland
SOURCE: Applied and Environmental Microbiology (2001), 67(10), 4638-4647
CODEN: AEMIDF; ISSN: 0099-2240
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Cyanobacteria of the genus Nodularia form toxic blooms in brackish waters worldwide. In addn., Nodularia spp. are found in benthic, periphytic, and soil habitats. The majority of the planktic isolates produce a pentapeptide hepatotoxin nodularin. We examd. the morphol., toxicol., and mol. characters of 18 nodularin-producing and nontoxic Nodularia strains to find appropriate markers for distinguishing the toxic strains from the nontoxic ones in field samples. After classical taxonomy, the examd. strains were identified as Nodularia sp., Nodularia spumigena, N. baltica, N. harveyana, and N. sphaerocarpa. Morphol. characters were ambiguous in terms of distinguishing between the toxic and the nontoxic strains. DNA sequences from the short 16S-23S rRNA internally transcribed spacer (ITS1-S) and from the phycocyanin operon intergenic spacer and its flanking regions (PC-**IGS**) were different for the toxic and the nontoxic strains. Phylogenetic anal. of the ITS1-S and PC-**IGS** sequences from strains identified as N. spumigena, and N. baltica, and N. litorea indicated that the division of the planktic Nodularia into the three species is not supported by the ITS1-S and PC-**IGS** sequences. However, the ITS1-S and PC-**IGS** sequences supported the sepn. of strains designated N. harveyana and N. sphaerocarpa from one another and the planktic strains. HaeIII digestion of PCR amplified PC-**IGS** regions of all examd. 186 Nodularia filaments collected from the Baltic Sea produced a digestion pattern similar to that found in toxic isolates. Our results suggest that only one planktic Nodularia species is present in the Baltic Sea plankton and that it is nodularin producing.

IT **118399-22-7**, Nodularin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Black Sea Nodularia producing; diversity of toxic and nontoxic Nodularia isolates (cyanobacteria) and filaments from the Baltic Sea)

RN 118399-22-7 HCAPLUS

CN Cyclo[L-arginyl-(2S,3S,4E,6E,8S,9S)-3-amino-9-methoxy-2,6,8-trimethyl-10-phenyl-4,6-decadienoyl-D-.gamma.-glutamyl-(2Z)-2-(methylamino)-2-butenoyl-(3S)-3-methyl-D-.beta.-aspartyl] (9CI) (CA INDEX NAME)



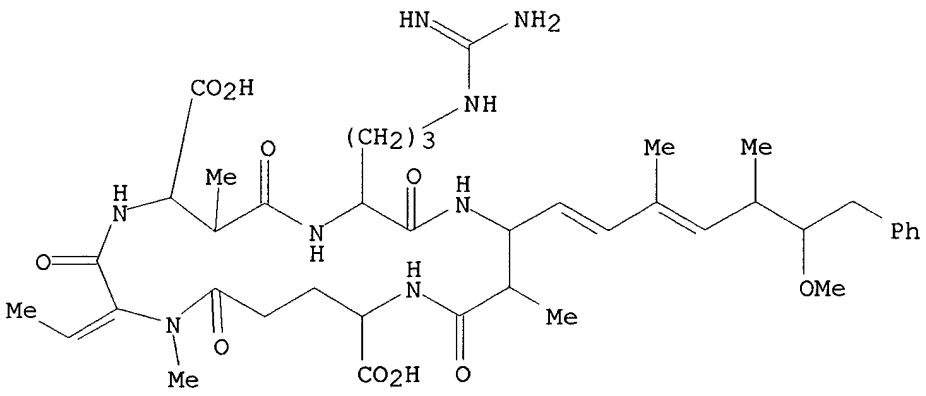
REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 13 OF 33 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:731800 HCAPLUS
DOCUMENT NUMBER: 135:299648
TITLE: Multidimensional Biochemical Detection of Microcystins in Liquid Chromatography
AUTHOR(S): Zeck, Anne; Weller, Michael G.; Niessner, Reinhard
CORPORATE SOURCE: Institute of Hydrochemistry, Technical University of Munich, Munich, D-81377, Germany
SOURCE: Analytical Chemistry (2001), 73(22), 5509-5517
CODEN: ANCHAM; ISSN: 0003-2700
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The coupling of **antibody**-, receptor-, or enzyme-based inhibition assays postcolumn to chromatog. systems provides biol. detectors with extraordinary high sensitivity and specificity. Three monoclonal **antibodies** (MC10E7, AD4G2, M8H5) directed against microcystins and protein phosphatase 1 (PP1) were used as off-line detectors for the HPLC sepn. of microcystins and nodularin in comparison to UV detection. For HPLC/**ELISA** coupling using **antibody** MC10E7, a detection limit of 0.04 ng microcystin-LR was achieved. The provisional guideline value for microcystin-LR (1 .mu.g/L, WHO) could be monitored without prior sample concn., in contrast to UV detection. Quantification of microcystin-LR and two cross-reactants was demonstrated. Furthermore, cross-reactivity or enzyme inhibition of new microcystins, only available in small amts., can be detd. by this method. Using a cyanobacterial ext., HPLC/**ELISA** coupling was compared to HPLC/UV and electrospray ionization mass spectrometry (ESI-TOFMS).

IT **118399-22-7**, Nodularin
RL: ANT (Analyte); ANST (Analytical study)
(multidimensional biochem. detection of microcystins in liq. chromatog.)

RN 118399-22-7 HCAPLUS
CN Cyclo[L-arginyl-(2S,3S,4E,6E,8S,9S)-3-amino-9-methoxy-2,6,8-trimethyl-10-phenyl-4,6-decadienoyl-D-.gamma.-glutamyl-(2Z)-2-(methylamino)-2-butenoyl-(3S)-3-methyl-D-.beta.-aspartyl] (9CI) (CA INDEX NAME)



REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 14 OF 33 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:580652 HCAPLUS
DOCUMENT NUMBER: 135:191533
TITLE: Time-dependent accumulation of cyanobacterial hepatotoxins in flounders (Platichthys flesus) and mussels (Mytilus edulis) from the Northern Baltic Sea
AUTHOR(S): Sipia, Vesa O.; Kankaanpaa, Harri T.; Flinkman, Juha; Lahti, Kirsti; Meriluoto, Jussi A. O.
CORPORATE SOURCE: Finnish Institute of Marine Research, Helsinki, 00931, Finland
SOURCE: Environmental Toxicology (2001), 16(4), 330-336
CODEN: ETOXFH; ISSN: 1520-4081
PUBLISHER: John Wiley & Sons, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

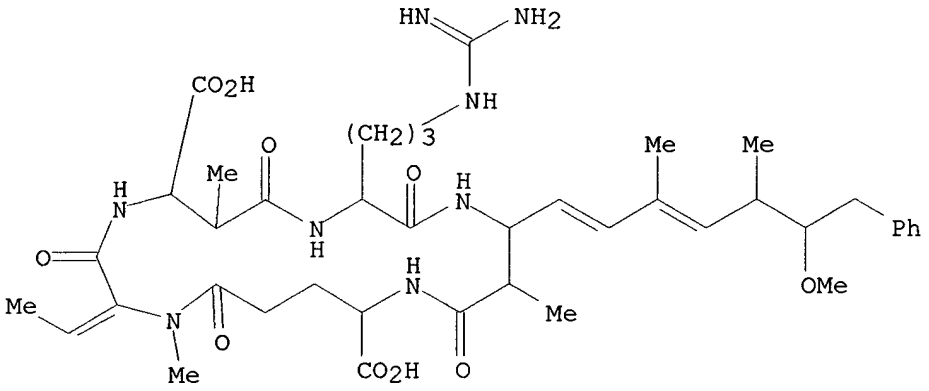
AB There is only limited information about the accumulation of algal toxins in aquatic organisms in the Baltic Sea. In this study the authors measured total cyanobacterial hepatotoxin levels in blue mussel (Mytilus edulis) and flounderi (Platichthys flesus) tissues. Flounder were caught with gillnets from the western Gulf of Finland during July and August 1999. Blue mussels were collected from an enclosure at 3 m depth and from an artificial reef (wreck, 25-35 m depth) in the western Gulf of Finland between June and Sept. 1999. Flounder liver and muscle samples and soft tissues of mussels were analyzed for the cyanobacterial hepatotoxins (nodularin, NODLN and/or microcystins, MCs) using an **ELISA** (**ELISA**). Results showed a time-dependent accumulation of hepatotoxins in flounder and mussels. In flounder, the max. concn. 399 .+-. 5 (sd) ng NODLN or MC/g dry wt. (dw) was found in the liver of specimens caught on 21 August 1999. No hepatotoxins were detected in muscle samples. The max. concn. of 2150 ng .+-. 60 (sd) ng hepatotoxin/g dw was found in the mussel soft tissues collected on 20 August 1999. Temporal NODLN or MC trends indicated depuration of cyanobacterial hepatotoxin from mussels at surface level and an increase in NODLN or MC concns. in those from the sea bed. These studies showed that despite the low cyanobacteria cell nos. the cyanobacterial hepatotoxins can accumulate in flounder and mussels. This may allow the further transfer of cyanobacterial hepatotoxins in the food web.

IT **118399-22-7,** nodularin

RL: ADV (Adverse effect, including toxicity); BIOL (Biological study) (cyanobacterial hepatotoxins accumulation (uptake) in flounders (Platichthys flesus) and mussels (Mytilus edulis) from the Northern Baltic Sea)

RN 118399-22-7 HCAPLUS

CN Cyclo[L-arginyl-(2S,3S,4E,6E,8S,9S)-3-amino-9-methoxy-2,6,8-trimethyl-10-phenyl-4,6-decadienoyl-D-.gamma.-glutamyl-(2Z)-2-(methylamino)-2-butenoyl-(3S)-3-methyl-D-.beta.-aspartyl] (9CI) (CA INDEX NAME)



REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 15 OF 33 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2001:556241 HCAPLUS

DOCUMENT NUMBER: 135:268419

TITLE: Production and specificity of monoclonal **antibodies** against nodularin conjugated through N-methyldehydrobutyrine

AUTHOR(S): Mikhailov, A.; Harmala-Brasken, A.-S.; Polosukhina, E.; Hanski, A.; Wahlsten, M.; Sivonen, K.; Eriksson, J. E.

CORPORATE SOURCE: Turku Centre for Biotechnology, Turku, FIN-20521, Finland

SOURCE: Toxicon (2001), 39(10), 1453-1459
CODEN: TOXIA6; ISSN: 0041-0101

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

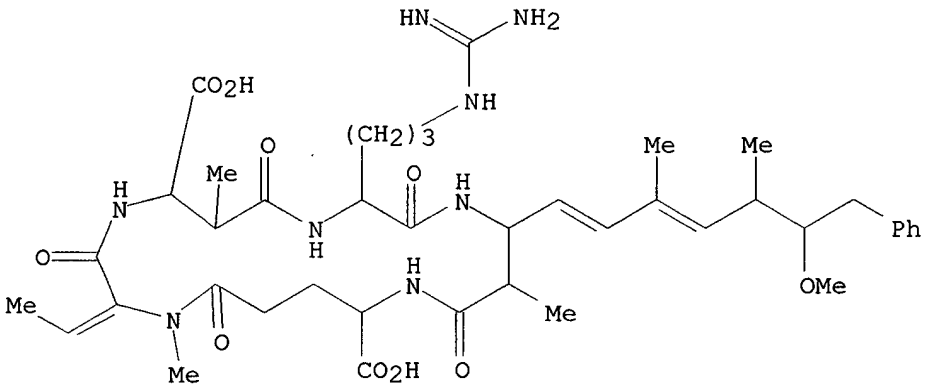
AB Nodularin (Nod) is a cyclic pentapeptide hepatotoxin produced by the cyanobacterial genus Nodularia living in brackish waters and coastal lagoons. The toxicity of Nod is due to specific inhibition of the type-1 and type-2A intracellular protein phosphatases (PP1 and PP2A, resp.). The authors have developed a monoclonal **antibody** against Nod using chem. modification (aminoethylation) of one of its core amino acids, N-methyldehydrobutyrine. The developed **antibody** is highly specific for Nod, with negligible reactivity to the closely related cyanobacterial toxin microcystin (MC). The monoclonal **antibody** was employed for quant. competitive **ELISA** assay. The anal. sensitivity of the assay was up to 0.2 ng/mL. Comparison of the developed **ELISA** test with HPLC-based measurements of Nod, with both lab. and

field samples, showed a good correspondence between the results yielded by these two methods. The **antibodies** developed by this technique provide means for developing extremely sensitive and specific anal. assays for direct measurement of nodularin and related toxins in cyanobacterial or water samples.

IT **118399-22-7,** Nodularin
RL: ADV (Adverse effect, including toxicity); ANT (Analyte); POL (Pollutant); ANST (Analytical study); BIOL (Biological study); OCCU (Occurrence)
(monoclonal **antibodies** against nodularin conjugated through N-methyldehydrobutyrine prodn.)

RN 118399-22-7 HCAPLUS

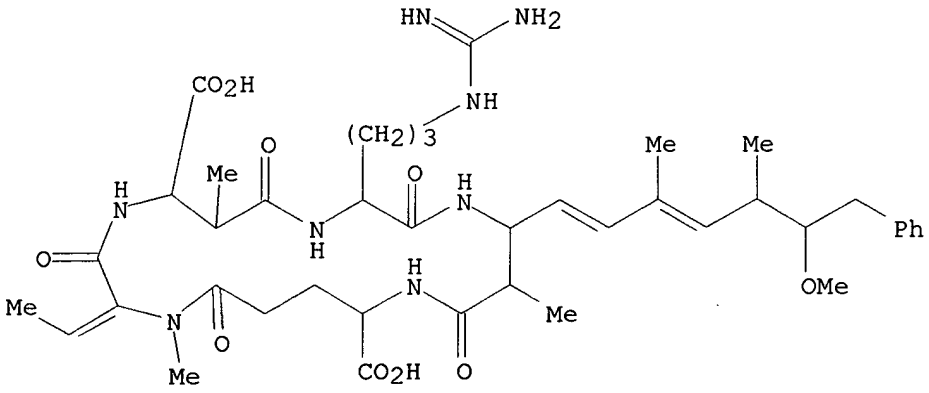
CN Cyclo[L-arginyl-(2S,3S,4E,6E,8S,9S)-3-amino-9-methoxy-2,6,8-trimethyl-10-phenyl-4,6-decadienoyl-D-.gamma.-glutamyl-(2Z)-2-(methylamino)-2-butenoyl-(3S)-3-methyl-D-.beta.-aspartyl] (9CI) (CA INDEX NAME)



IT **118399-22-7D,** Nodularin, conjugates with N-methyldehydrobutyrine
RL: ARU (Analytical role, unclassified); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); ANST (Analytical study); BIOL (Biological study); PROC (Process)
(monoclonal **antibodies** against nodularin conjugated through N-methyldehydrobutyrine prodn.)

RN 118399-22-7 HCAPLUS

CN Cyclo[L-arginyl-(2S,3S,4E,6E,8S,9S)-3-amino-9-methoxy-2,6,8-trimethyl-10-phenyl-4,6-decadienoyl-D-.gamma.-glutamyl-(2Z)-2-(methylamino)-2-butenoyl-(3S)-3-methyl-D-.beta.-aspartyl] (9CI) (CA INDEX NAME)



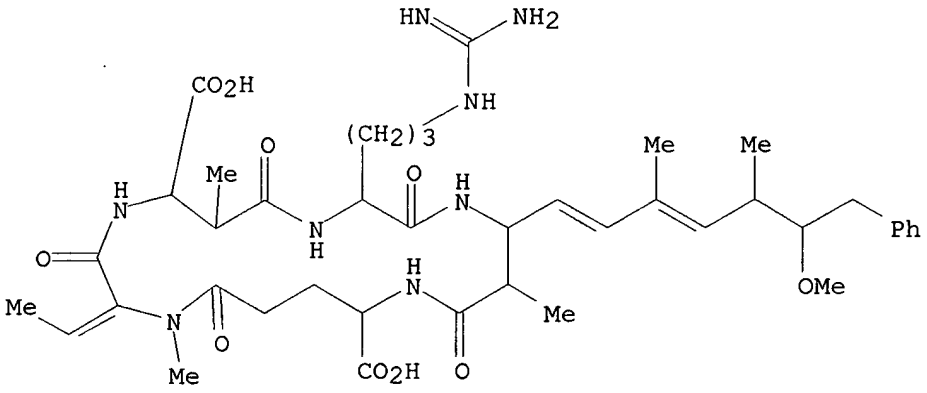
REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 16 OF 33 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:406704 HCAPLUS
DOCUMENT NUMBER: 135:88390
TITLE: Microcystin-induced down-regulation of lymphocyte functions through reduced IL-2 mRNA stability
AUTHOR(S): Yea, S. S.; Kim, H. M.; Oh, H.-M.; Paik, K.-H.; Yang, K.-H.
CORPORATE SOURCE: The Paik-Inje Memorial Institute for Biomedical Science, Inje University, Pusanjin-gu, Pusan, 614-735, S. Korea
SOURCE: Toxicology Letters (2001), 122(1), 21-31
CODEN: TOLED5; ISSN: 0378-4274
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Here we report that lymphocyte functions were down-regulated by cyanobacterial hepatotoxin microcystin. Treatment of three microcystin (MC) isotypes, MC-LR, MC-YR and nodularin, on B6C3F1 mouse splenocytes produced dose-dependent inhibition of in vitro polyclonal **antibody** response and lymphoproliferation to LPS. ConA-induced lymphoproliferative response was decreased by MC-YR and nodularin, but no significant effect was obsd. in the MC-LR treatment. I.p. administration of nodularin into B6C3F1 mice decreased humoral immune responses to sheep red blood cell (sRBC), and the inhibitory effect became severe when hepatic uptake of nodularin was blocked by rifampicin. Each MC 1 .mu.M suppressed phorbol 12-myristate 13-acetate (PMA) plus ionomycin-induced IL-2 mRNA expression in splenocytes and thymocytes, but not in EL-4 mouse thymoma cells. To further characterize the mechanism for the reduced IL-2 mRNA level, IL-2 mRNA stability was measured using RT-PCR. Deprivation of PMA/ionomycin stimuli from activated splenocytes and blockade of new transcription resulted in destabilization of IL-2 mRNA, which was accelerated by MC treatment. These results demonstrated that MC down-regulated lymphocyte functions and the **immunosuppression** was mediated, at least in part, through decreased IL-2 mRNA stability.

IT **118399-22-7**, Nodularin
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study) (microcystin-induced down-regulation of lymphocyte functions through reduced IL-2 mRNA stability)

RN 118399-22-7 HCAPLUS
CN Cyclo[L-arginyl-(2S,3S,4E,6E,8S,9S)-3-amino-9-methoxy-2,6,8-trimethyl-10-phenyl-4,6-decadienoyl-D-.gamma.-glutamyl-(2Z)-2-(methylamino)-2-butenoyl-(3S)-3-methyl-D-.beta.-aspartyl] (9CI) (CA INDEX NAME)



REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 17 OF 33 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:250821 HCAPLUS
DOCUMENT NUMBER: 134:362553
TITLE: Detection of nodularin in flounders and cod from the Baltic Sea
AUTHOR(S): Sipia, Vesa; Kankaanpaa, Harri; Lahti, Kirsti; Carmichael, Wayne W.; Meriluoto, Jussi
CORPORATE SOURCE: Finnish Institute of Marine Research, Helsinki, 00931, Finland
SOURCE: Environmental Toxicology (2001), 16(2), 121-126
CODEN: ETOXFH; ISSN: 1520-4081
PUBLISHER: John Wiley & Sons, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

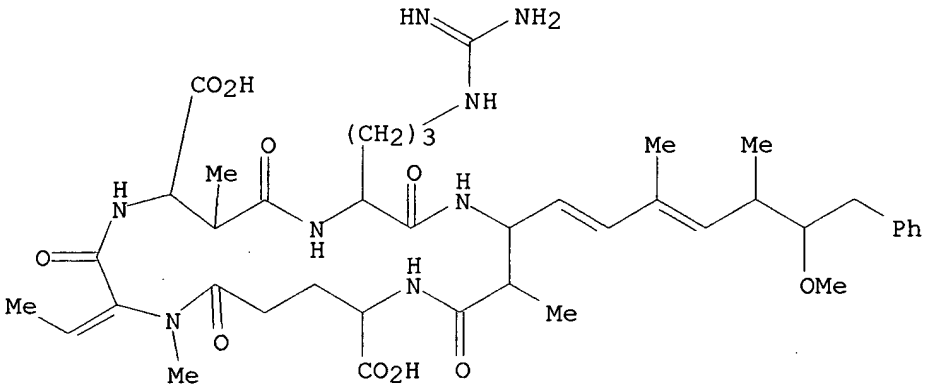
AB The brackish water cyanobacterium Nodularia spumigena regularly forms water blooms in the Baltic Sea. Many N. spumigena strains can produce nodularin, a hepatotoxic pentapeptide, which caused several animal poisonings in the Baltic Sea area. To improve the understanding of nodularin bioaccumulation in aquatic organisms this study measured nodularin in flounder and cod caught from the Baltic Sea. Flounders were collected from the western Gulf of Finland in July 1996, Sept. 1997, and Sept. 1998, and from the Gulf of Bothnia in August 1997 and Sept. 1998. Flounders were also collected from the coastal areas of Sweden in the Baltic Proper during Sept. 1998. Cod were caught from the southern Baltic Sea in August 1998. Livers and muscles of the 1997 fish were isolated, extd., and analyzed for nodularin using HPLC and **ELISA** and protein phosphatase 1 (PP1) inhibition assay. Approx. 30-70 ng of nodularin/g dry wt. (max. value 140 ng/g) were found in the liver tissue samples by **ELISA** and PP1 inhibition. These concns. were below the detection limit of HPLC. PP1 assay showed inhibition also in muscle samples, but this may due to other compds. present in the muscle exts. rather than NODLN or due to matrix interference. The recovery of

nodularin from liver tissue with **ELISA** and PP1 assays was about 30%. Nodularin concns. in samples are not cor. for recovery. Although the concns. of nodularin found in this study are low further studies of nodularin are needed to assess possible bioaccumulation in brackish water food webs.

IT **118399-22-7**, Nodularin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(detection of nodularin in flounders and cod)

RN 118399-22-7 HCAPLUS

CN Cyclo[L-arginyl-(2S,3S,4E,6E,8S,9S)-3-amino-9-methoxy-2,6,8-trimethyl-10-phenyl-4,6-decadienoyl-D-.gamma.-glutamyl-(2Z)-2-(methylamino)-2-butenoyl-(3S)-3-methyl-D-.beta.-aspartyl] (9CI) (CA INDEX NAME)



REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 18 OF 33 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:185805 HCAPLUS
DOCUMENT NUMBER: 134:221452
TITLE: Congener-independent detection of microcystin and nodularin congeners
INVENTOR(S): Dietrich, Daniel R.; Fischer, Werner; Chamberlin, A. Richard; Aggen, James B.; Garthwaite, Ian; Miles, Christopher O.; Ross, Kathryn M.; Towers, Noale
PATENT ASSIGNEE(S): Regent of the University of California, USA; New Zealand Agricultural Research
SOURCE: PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001018059	A2	20010315	WO 2000-EP8711	20000906
WO 2001018059	A3	20010802		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,

HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1210373 A2 20020605 EP 2000-956519 20000906
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL

PRIORITY APPLN. INFO.: EP 1999-116881 A 19990906
WO 2000-EP8711 W 20000906

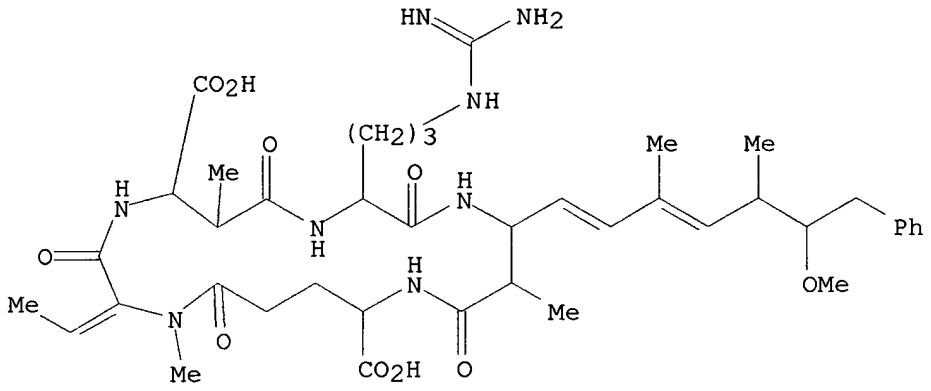
OTHER SOURCE(S): MARPAT 134:221452

AB The present invention relates to a proteinaceous compd. or functionally active deriv. or part thereof having a binding site for a group represented by formula (I) which is part of a group of toxins derived from various cyanobacteria, to a method for its prodn., to diagnostic kits and to an affinity matrix (e.g. for use in **immunoaffinity** columns, online detection and purifications devices) contg. the proteinaceous compd. as well as to methods for substantially decreasing the amt. of a compd. contg. the group represented by formula (I) in fluids or for concg. compds., e.g. toxins, contg. the group represented by formula (I) from fluids such as crude water samples, exts. of algae or other tissue samples, e.g. to det. toxin concns.

IT **118399-22-7**, Nodularin
RL: ANT (Analyte); BSU (Biological study, unclassified); PRP (Properties); ANST (Analytical study); BIOL (Biological study)
(**antibodies** for **immunoaffinity** detection of microcystin and nodularin congener-contg. toxin in waters)

RN 118399-22-7 HCAPLUS

CN Cyclo[L-arginyl-(2S,3S,4E,6E,8S,9S)-3-amino-9-methoxy-2,6,8-trimethyl-10-phenyl-4,6-decadienoyl-D-.gamma.-glutamyl-(2Z)-2-(methylamino)-2-butenoyl-(3S)-3-methyl-D-.beta.-aspartyl] (9CI) (CA INDEX NAME)



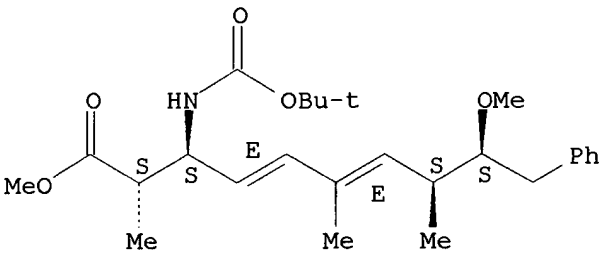
IT **134440-91-8**
RL: RCT (Reactant); RACT (Reactant or reagent)
(**antibodies** for **immunoaffinity** detection of microcystin and nodularin congener-contg. toxin in waters)

RN 134440-91-8 HCAPLUS

CN 4,6-Decadienoic acid, 3-[[(1,1-dimethylethoxy)carbonyl]amino]-9-methoxy-

2,6,8-trimethyl-10-phenyl-, methyl ester, (2S,3S,4E,6E,8S,9S)- (9CI) (CA INDEX NAME)

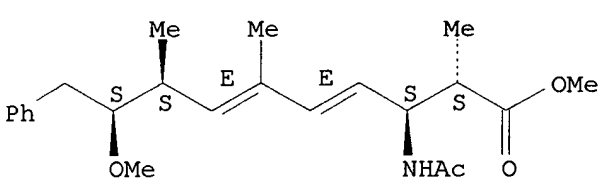
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



IT **329791-61-9P 329791-62-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(**antibodies** for **immunoaffinity** detection of microcystin and nodularin congener-contg. toxin in waters)

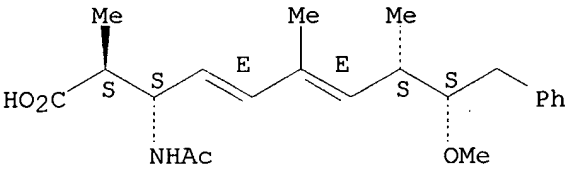
RN 329791-61-9 HCAPLUS
CN 4,6-Decadienoic acid, 3-(acetylamino)-9-methoxy-2,6,8-trimethyl-10-phenyl-, methyl ester, (2S,3S,4E,6E,8S,9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 329791-62-0 HCAPLUS
CN 4,6-Decadienoic acid, 3-(acetylamino)-9-methoxy-2,6,8-trimethyl-10-phenyl-, (2S,3S,4E,6E,8S,9S)- (9CI) (CA INDEX NAME)

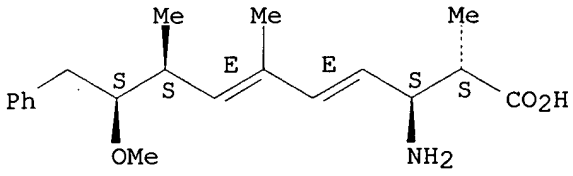
Absolute stereochemistry.
Double bond geometry as shown.



IT **126456-06-2**
RL: ANT (Analyte); BSU (Biological study, unclassified); PRP (Properties); ANST (Analytical study); BIOL (Biological study)
(toxin contg.; **antibodies** for **immunoaffinity** detection of microcystin and nodularin congener-contg. toxin in waters)

RN 126456-06-2 HCAPLUS
CN 4,6-Decadienoic acid, 3-amino-9-methoxy-2,6,8-trimethyl-10-phenyl-, (2S,3S,4E,6E,8S,9S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



L12 ANSWER 19 OF 33 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:110653 HCAPLUS
DOCUMENT NUMBER: 134:306247
TITLE: Colorimetric **immuno**-protein phosphatase inhibition assay for specific detection of microcystins and nodularins of cyanobacteria
AUTHOR(S): Metcalf, James S.; Bell, Steven G.; Codd, Geoffrey A.
CORPORATE SOURCE: Department of Biological Sciences, University of Dundee, Dundee, DD1 4HN, UK
SOURCE: Applied and Environmental Microbiology (2001), 67(2), 904-909
CODEN: AEMIDF; ISSN: 0099-2240
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

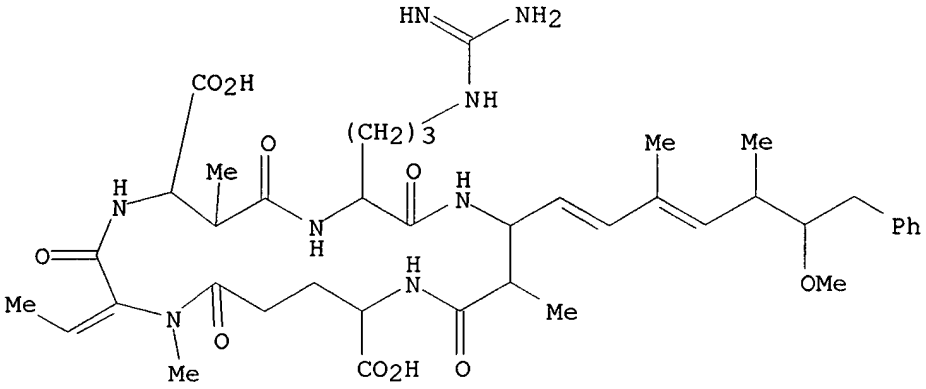
AB A novel **immunoassay** was developed for specific detection of cyanobacterial cyclic peptide hepatotoxins which inhibit protein phosphatases. **Immunoassay** methods currently used for microcystin and nodularin detection and anal. do not provide information on the toxicity of microcystin and/or nodularin variants. Furthermore, protein phosphatase inhibition-based assays for these toxins are not specific and respond to other environmental protein phosphatase inhibitors, such as okadaic acid, calyculin A, and tautomycin. We addressed the problem of specificity in the anal. of protein phosphatase inhibitors by combining **immunoassay**-based detection of the toxins with a colorimetric protein phosphatase inhibition system in a single assay, designated the colorimetric **immuno**-protein phosphatase inhibition assay (CIPPIA). Polyclonal **antibodies** against microcystin-LR were used in conjunction with protein phosphatase inhibition, which enabled seven purified microcystin variants (microcystin-LR, -D-Asp3-RR, -LA, -LF, -LY, -LW, and -YR) and nodularin to be distinguished from okadaic acid, calyculin A, and tautomycin. A range of microcystin- and nodularin-contg. lab. strains and environmental samples of cyanobacteria were assayed by CIPPIA, and the results showed good correlation ($R2 = 0.94$, $P < 0.00001$) with the results of high-performance liq. chromatog. with diode array detection for toxin anal. The CIPPIA procedure combines ease of use and detection of low concns. with toxicity assessment and specificity for anal. of microcystins and nodularins.

IT **118399-22-7**, Nodularin
RL: ANT (Analyte); ANST (Analytical study)

(colorimetric **immuno**-protein phosphatase inhibition assay for specific detection of microcystins and nodularins of cyanobacteria)

RN 118399-22-7 HCAPLUS

CN Cyclo[L-arginyl-(2S,3S,4E,6E,8S,9S)-3-amino-9-methoxy-2,6,8-trimethyl-10-phenyl-4,6-decadienoyl-D-.gamma.-glutamyl-(2Z)-2-(methylamino)-2-butenoyl-(3S)-3-methyl-D-.beta.-aspartyl] (9CI) (CA INDEX NAME)



REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 20 OF 33 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2001:43123 HCAPLUS

DOCUMENT NUMBER: 134:203532

TITLE: Using an **enzyme linked immunosorbent** assay (**ELISA**) and a protein phosphatase inhibition assay (PPIA) for the detection of microcystins and nodularins

AUTHOR(S): Carmichael, Wayne W.; An, Jisi

CORPORATE SOURCE: Department of Biological Sciences, Wright State University, Dayton, OH, 45435, USA

SOURCE: Natural Toxins (1999), 7(6), 377-385
CODEN: NATOEE; ISSN: 1056-9014

PUBLISHER: John Wiley & Sons Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

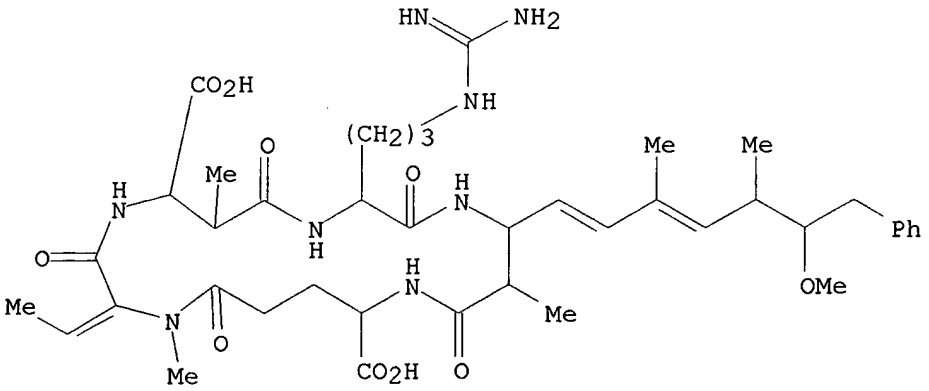
AB Cyanotoxins produced by cyanobacteria (blue-green algae) include potent neurotoxins and hepatotoxins. The hepatotoxins include cyclic peptide microcystins and nodularins plus the alkaloid cylindrospermopsins. Among the cyanotoxins the microcystins have proven to be the most widespread, and are most often implicated in animal and human poisonings. This paper presents a practical guide to two widely used methods for detecting and quantifying microcystins and nodularins in environmental samples: the **enzyme linked immunosorbent** assay (**ELISA**) and the protein phosphatase inhibition assay.

IT **118399-22-7**, Nodularin
RL: ANT (Analyte); ANST (Analytical study)
(**ELISA** and protein phosphatase inhibition assay for detection of microcystins and nodularins)

RN 118399-22-7 HCAPLUS

CN Cyclo[L-arginyl-(2S,3S,4E,6E,8S,9S)-3-amino-9-methoxy-2,6,8-trimethyl-10-

phenyl-4,6-decadienoyl-D-.gamma.-glutamyl-(2Z)-2-(methylamino)-2-butenoyl-(3S)-3-methyl-D-.beta.-aspartyl] (9CI) (CA INDEX NAME)



REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 21 OF 33 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:785087 HCAPLUS
DOCUMENT NUMBER: 134:143073
TITLE: Production and specificity of mono and polyclonal **antibodies** against microcystins conjugated through N-methyldehydroalanine
AUTHOR(S): Mikhailov, Andrey; Harmala-Brasken, Ann-Sofi; Meriluoto, Jussi; Sorokina, Yulia; Dietrich, Daniel; Eriksson, John E.
CORPORATE SOURCE: Turku Centre for Biotechnology, Turku, FIN-20521, Finland
SOURCE: Toxicon (2001), 39(4), 477-483
CODEN: TOXIA6; ISSN: 0041-0101
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

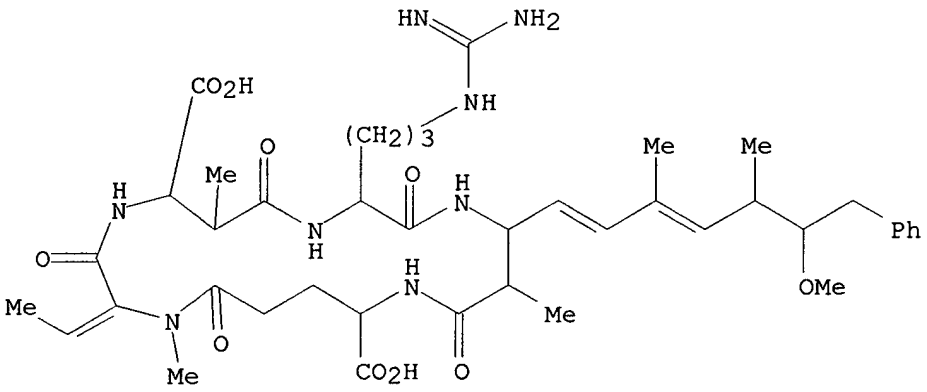
AB Microcystins (MCs) are a group of closely related toxic cyclic heptapeptides produced by common cyanobacteria (blue-green algae). Their toxicity is assocd. with specific inhibition of intracellular protein phosphatases type-1 and type-2A (PP1 and PP2A, resp.). The authors have developed a battery of **antibodies** to microcystins using chem. modification (aminoethylation) of one of its core amino acids, N-methyl-dehydroalanine. The developed **antibodies** displayed different reactivities to closely related MCs. Selected monoclonal **antibodies** were used for quant. competitive **ELISA** assays. The anal. sensitivity of these assays was up to 1 ng/mL. Comparison of the developed **ELISA** tests with HPLC-based measurements of MCs in lab. and field samples showed a good correspondence between the results yielded by these two methods. The **antibodies** developed by this technique provide the means for developing extremely sensitive and specific anal. assays for direct measurement of toxins in cyanobacterial or water samples.

IT **118399-22-7**, Nodularin
RL: ANT (Analyte); BPR (Biological process); BSU (Biological study,

unclassified); ANST (Analytical study); BIOL (Biological study); PROC (Process)
(prodn. and specificity of mono and polyclonal **antibodies** against microcystins conjugated through N-methyldehydroalanine)

RN 118399-22-7 HCAPLUS

CN Cyclo[L-arginyl-(2S,3S,4E,6E,8S,9S)-3-amino-9-methoxy-2,6,8-trimethyl-10-phenyl-4,6-decadienoyl-D-.gamma.-glutamyl-(2Z)-2-(methylamino)-2-butenoyl-(3S)-3-methyl-D-.beta.-aspartyl] (9CI) (CA INDEX NAME)



REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 22 OF 33 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2000:649479 HCAPLUS

DOCUMENT NUMBER: 133:359916

TITLE: Modulation of Human Polymorphonuclear Leukocyte Adherence by Cyanopeptide Toxins

AUTHOR(S): Hernandez, Mercedes; Macia, Manuel; Padilla, Carlos; Del Campo, Francisca F.

CORPORATE SOURCE: Departamento de Biologia Animal II, Facultad de Biologia, Universidad Complutense de Madrid, Madrid, 28040, Spain

SOURCE: Environmental Research (2000), 84(1), 64-68
CODEN: ENVRAL; ISSN: 0013-9351

PUBLISHER: Academic Press

DOCUMENT TYPE: Journal

LANGUAGE: English

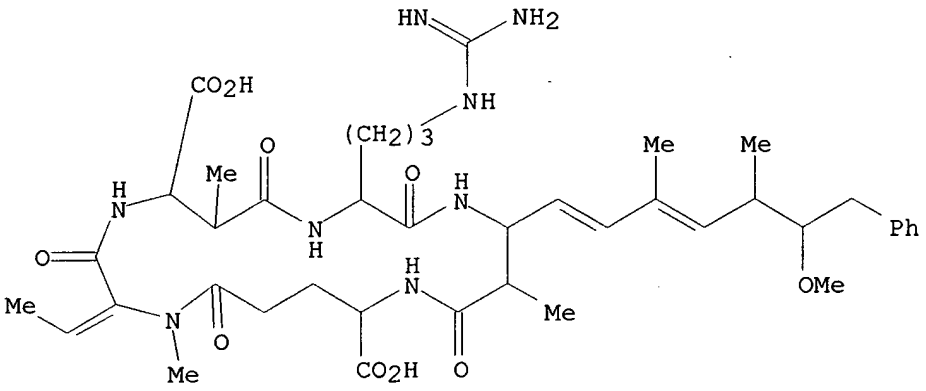
AB The oligopeptides microcystins and nodularins are the most common and abundant cyanotoxins present in diverse water systems. They cause different illnesses in animal and humans, sometimes leading to death, and are responsible for severe environmental problems. Here both microcystin-LR and N. spumigena nodularin (Nod) significantly enhance the early spontaneous adherence of peripheral polymorphonuclear leukocytes (PMNs) over the concn. range 10-11-10-9 M. However, neither of them affect significantly the late spontaneous adherence or the early or late PMN-stimulated adherence (when cells are treated with formyl-methionyl-leucyl-phenylalanine). Since PMN adherence is a key step in the immune response, the authors' data clearly indicate for the first time the **immunomodulatory** capacity of cyanopeptide toxins. The low concns. at which the adherence modulation occurs are similar to the physiol.

concns. for natural mammalian peptide hormones. Such concns. are well below those recommended by other authors and World Health Organization in terms of risk assessment as safe for drinking water (8 .times. 10-10 to 10-9 M). (c) 2000 Academic Press.

IT **118399-22-7**, Cyclo[L-arginyl-(2S,3S,4E,6E,8S,9S)-3-amino-9-methoxy-2,6,8-trimethyl-10-phenyl-4,6-decadienoyl-D-.gamma.-glutamyl-(2Z)-2-(methylamino)-2-butenoyl-(3S)-3-methyl-D-.beta.-aspartyl]
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(modulation of human polymorphonuclear leukocyte adherence by microcystin LR and nodularin)

RN 118399-22-7 HCAPLUS

CN Cyclo[L-arginyl-(2S,3S,4E,6E,8S,9S)-3-amino-9-methoxy-2,6,8-trimethyl-10-phenyl-4,6-decadienoyl-D-.gamma.-glutamyl-(2Z)-2-(methylamino)-2-butenoyl-(3S)-3-methyl-D-.beta.-aspartyl] (9CI) (CA INDEX NAME)



REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 23 OF 33 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2000:411790 HCAPLUS

DOCUMENT NUMBER: 133:48547

TITLE: Production of novel polyclonal **antibodies** against the cyanobacterial toxin microcystin-LR and their application for the detection and quantification of microcystins and nodularin

AUTHOR(S): Metcalf, J. S.; Bell, S. G.; Codd, G. A.

CORPORATE SOURCE: Department of Biological Sciences, University of Dundee, Dundee, DD1 4HN, UK

SOURCE: Water Research (2000), 34(10), 2761-2769
CODEN: WATRAG; ISSN: 0043-1354

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

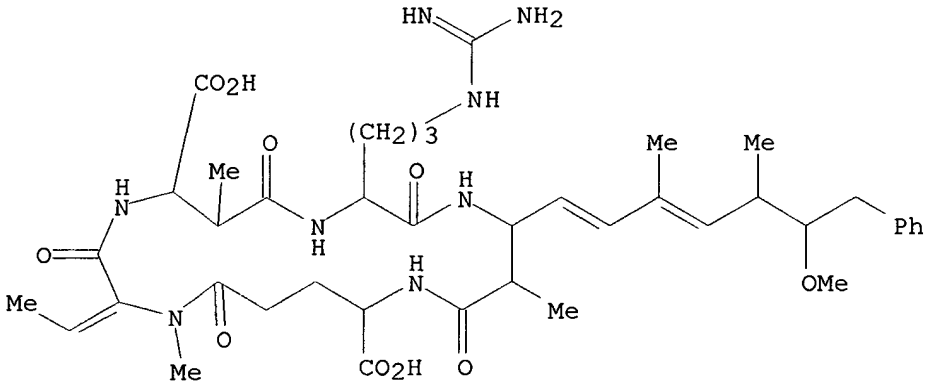
AB A conjugation method was developed by linking the **hapten**, the cyanobacterial hepatotoxin microcystin-LR, via 2-mercaptoethylamine to keyhole limpet hemocyanin. Polyclonal antisera were raised against this conjugate and an indirect competitive **immunoassay** (**ELISA**) developed which can detect purified microcystin-LR and the toxin in exts. of cyanobacteria from fresh-, brackish and marine waters. The cross-reactivity of the microcystin-LR **antibodies** was studied

with a range of purified microcystin variants (-LR, -LA, -LY, -LW, -LF, -D-Asp3-RR, and -Asp3(Z)-Dhb7-HtyR) and nodularin. The **antibodies** cross-reacted well with all microcystin and nodularin variants. The microcystin-LA was the most readily detectable, followed by microcystins-LR, -LF, -LW, -D-Asp3-RR, -LY, nodularin and microcystin-Asp3(Z)-Dhb7-HtyR. Exts. from several genera of cyanobacteria were studied by the **ELISA** and the results compared to HPLC with diode array detection (DAD). By the **ELISA** procedure, 60% were pos., compared to detection of microcystins in 45% of the samples by HPLC-DAD. Anal. of microcystin-LR equiv. by **ELISA** and HPLC-DAD showed good correlation (R = 0.96, p <1 .times. 10-10). The application of the anti-microcystin-LR **antibodies** for the detection and quantification of microcystins and nodularin in environmental water samples is discussed.

IT **118399-22-7**, Nodularin
RL: ANT (Analyte); ANST (Analytical study)
(prodn. of polyclonal **antibodies** against cyanobacterial toxin microcystin-LR and application to detection and quantification of microcystins and nodularin)

RN 118399-22-7 HCAPLUS

CN Cyclo[L-arginyl-(2S,3S,4E,6E,8S,9S)-3-amino-9-methoxy-2,6,8-trimethyl-10-phenyl-4,6-decadienoyl-D-.gamma.-glutamyl-(2Z)-2-(methylamino)-2-butenoyl-(3S)-3-methyl-D-.beta.-aspartyl] (9CI) (CA INDEX NAME)



REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 24 OF 33 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2000:411775 HCAPLUS
DOCUMENT NUMBER: 133:34198
TITLE: Visual detection of cyanobacterial hepatotoxins by thin-layer chromatography and application to water analysis
AUTHOR(S): Pelander, Anna; Ojanpera, Ilkka; Lahti, Kirsti; Niinivaara, Kauko; Vuori, Erkki
CORPORATE SOURCE: Department of Forensic Medicine, Forensic Toxicology Division, University of Helsinki, Helsinki, FIN-00014, Finland
SOURCE: Water Research (2000), 34(10), 2643-2652
CODEN: WATRAG; ISSN: 0043-1354

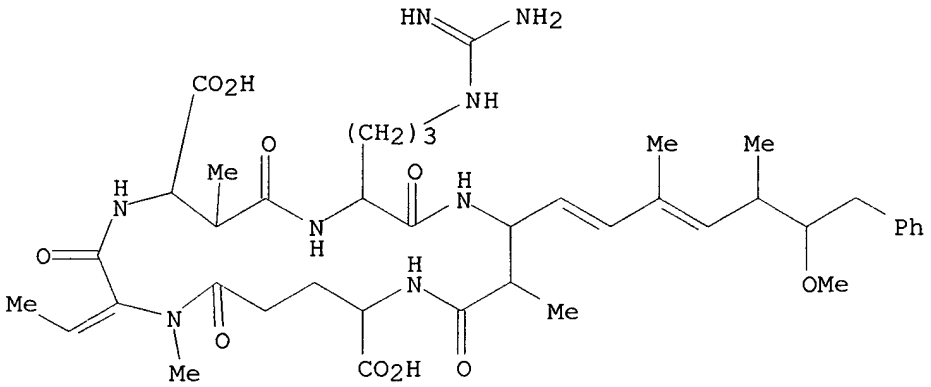
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Visualization reactions for the thin-layer chromatog. (TLC) anal. of cyanobacterial hepatotoxins microcystins and nodularin were studied. Of the 17 potential reactions tested, 9 yielded either colored, fluorescent, or both products with the purified toxins. The detection limit of pure microcystin-LR in these reactions ranged from 10 to 250 ng. Feasibility of the reactions for water anal. was studied in fortified 50-500 mL water samples. The best result was obtained with N,N-dimethyl-1,4-phenylendiammonium dichloride (N,N-DPDD). A water anal. method meeting the WHO drinking water guideline concn. value, 1 .mu.g/L microcystin-LR, was developed using N,N-DPDD. The method was tested by analyzing blind 38 authentic natural water samples, studied earlier by the **ELISA** and protein phosphatase inhibition assay (PP). In 31 samples the results of all 3 methods were consistent. Two apparently false pos. results were obtained by TLC, and in 2 samples results were pos. by **ELISA** and TLC but not PP. In one sample the result was pos. by PP but not **ELISA** or TLC. Two samples were pos. by **ELISA** and PP and not TLC, but a full 50 mL sample for TLC was not available in these cases, thus making the detection limit higher. Results suggest that the present TLC method is comparable with the **ELISA** and PP assays and TLC can be used for cost-effective monitoring of water samples according to the WHO guidelines.

IT **118399-22-7**, Nodularin
RL: ANT (Analyte); POL (Pollutant); ANST (Analytical study); OCCU (Occurrence)
(visual detection of cyanobacterial hepatotoxins by thin-layer chromatog. and application to water anal.)

RN 118399-22-7 HCAPLUS

CN Cyclo[L-arginyl-(2S,3S,4E,6E,8S,9S)-3-amino-9-methoxy-2,6,8-trimethyl-10-phenyl-4,6-decadienoyl-D-.gamma.-glutamyl-(2Z)-2-(methylamino)-2-butenoyl-(3S)-3-methyl-D-.beta.-aspartyl] (9CI) (CA INDEX NAME)



REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 25 OF 33 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:244414 HCAPLUS
DOCUMENT NUMBER: 133:85412

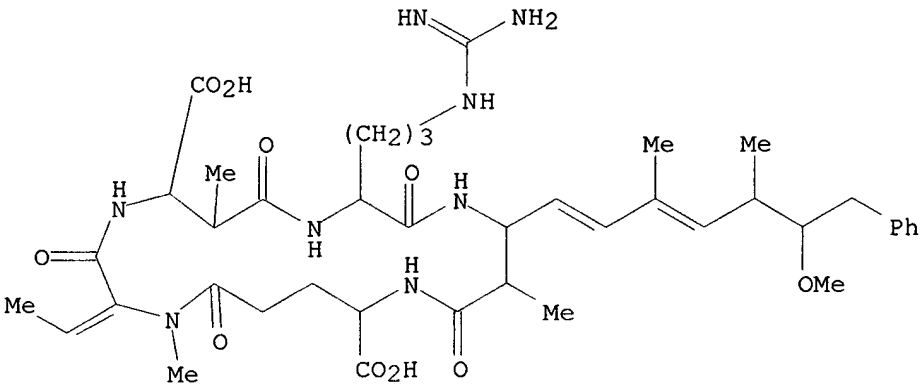
TITLE: Isolation and detection of microcystins and nodularins, cyanobacterial peptide hepatotoxins
AUTHOR(S): Meriluoto, Jussi; Lawton, Linda; Harada, Ken-Ichi
CORPORATE SOURCE: Department of Biochemistry and Pharmacy, Abo Akademi University, Turku, Finland
SOURCE: Methods in Molecular Biology (Totowa, New Jersey) (2000), 145(Bacterial Toxins), 65-87
CODEN: MMBIED; ISSN: 1064-3745
PUBLISHER: Humana Press Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Toxin producers, structure, nomenclature, isolation methods, anal. of microcystins, microscopy of cyanobacteria, isolation of microcystin-LR and -RR variants and nodularin-R, flash chromatog. and HPLC in isolation of cyanobacterial toxins, spectrophotometric anal. of pure microcystins, amino acid anal. of purified cyanobacterial toxins, isocratic reversed-phase HPLC of microcystin -LA, -LR, -YR, -RR and nodularin-R, reversed-phase gradient HPLC at low pH of cyanobacterial toxins, mouse bioassay, Artemia salina bioassay, protein phosphatase inhibition assay, **ELISA** of cyanobacterial toxins, and toxicity were discussed.

IT **118399-22-7**, Nodularin
RL: ADV (Adverse effect, including toxicity); ANT (Analyte); BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); ANST (Analytical study); BIOL (Biological study); OCCU (Occurrence)
(microcystins and nodularins, cyanobacterial peptide hepatotoxins toxicity, bioassay, isolation and anal. (detection))

RN 118399-22-7 HCAPLUS

CN Cyclo[L-arginyl-(2S,3S,4E,6E,8S,9S)-3-amino-9-methoxy-2,6,8-trimethyl-10-phenyl-4,6-decadienoyl-D-.gamma.-glutamyl-(2Z)-2-(methylamino)-2-butenoyl-(3S)-3-methyl-D-.beta.-aspartyl] (9CI) (CA INDEX NAME)



REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 26 OF 33 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:235037 HCAPLUS
DOCUMENT NUMBER: 133:29419
TITLE: Generation of **antibodies** directed against the low-**immunogenic** peptide-toxins

microcystin-LR/RR and nodularin

AUTHOR(S): Baier, W.; Loleit, M.; Fischer, B.; Jung, G.; Neumann, U.; Weiss, M.; Weckesser, J.; Hoffmann, P.; Bessler, W. G.; Mittenbuhler, K.

CORPORATE SOURCE: Institut fur Immunobiologie der Universitat, Freiburg, D-79104, Germany

SOURCE: International Journal of Immunopharmacology (2000), 22(5), 339-353
CODEN: IJIMDS; ISSN: 0192-0561

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

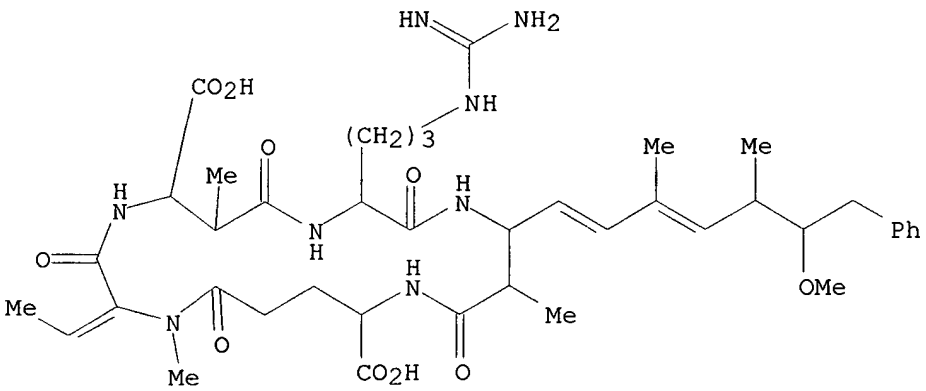
LANGUAGE: English

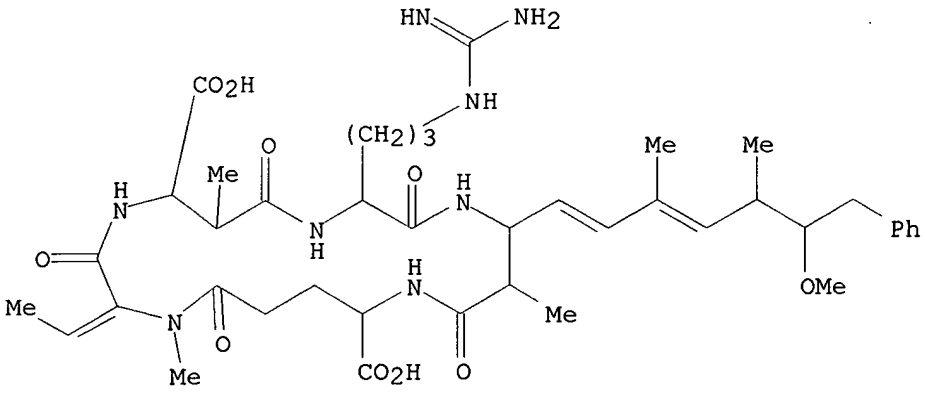
AB The prepn. of **antibodies** against the liver toxin microcystin, as described here, is of major importance for its detection and purifn. in food and water, and for a therapeutic approach to neutralize the toxin by passive immunization. Microcystin-LR (MLR) and microcystin-RR (MRR) were purified from cyanobacterial cell materials by extn., Sephadex LH-20-, ODS silica gel-, ionic exchange and RP-HPLC-chromatog. To reduce the toxicity for parenteral administration, microcystins were coupled by the carbodiimide method to poly-L-lysine (PLL50,000). Mice and rabbits were immunized with the conjugates in the presence of two lipopeptide **immunoadjuvants** (P3CSK4 and P3CS-Th). High MLR-specific **antibody** levels were obsd. after parenteral coadministration of **antigen** and lipopeptides, whereas no anti-MLR **antibodies** were obtained with free microcystin or the microcystin-PLL50,000-conjugate in the absence of lipopeptide. In oral immunization, coadministration of **antigen** and adjuvants resulted in an accelerated development of anti MLR-specific **antibodies** and high **antibody** levels. Using the antisera, the authors could detect different microcystins and nodularin down to a concn. range of 10-50 ng/mL by a competitive inhibition **ELISA**; detection of microcystins in crude cell prepns. was also possible. Furthermore, microcystins from different sources could be detected and discriminated from cyclic cyanopeptolines.

IT **118399-22-7**, Nodularin
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(cross-reactivity with **antibodies** to microcystins)

RN 118399-22-7 HCAPLUS

CN Cyclo[L-arginyl-(2S,3S,4E,6E,8S,9S)-3-amino-9-methoxy-2,6,8-trimethyl-10-phenyl-4,6-decadienoyl-D-.gamma.-glutamyl-(2Z)-2-(methylamino)-2-butenoyl-(3S)-3-methyl-D-.beta.-aspartyl] (9CI) (CA INDEX NAME)





REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

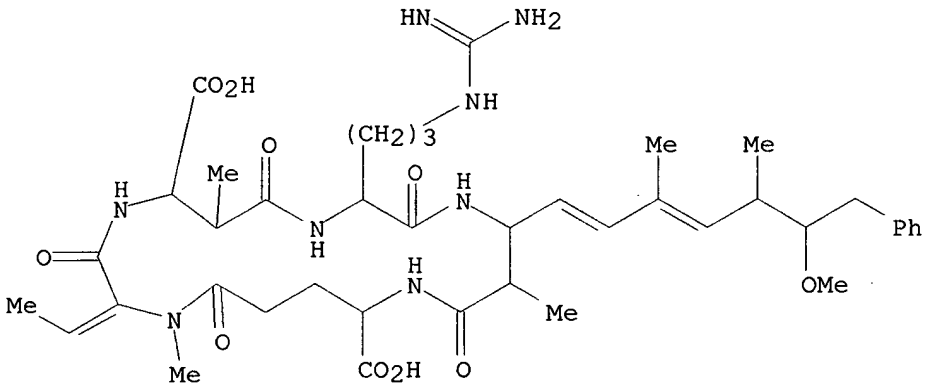
L12 ANSWER 27 OF 33 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:536396 HCAPLUS
DOCUMENT NUMBER: 131:282619
TITLE: Effect of nodularin on the expression of glutathione S-transferase placental form and proliferating cell nuclear **antigen** in N-nitrosodiethylamine initiated hepatocarcinogenesis in the male Fischer 344 rat
AUTHOR(S): Song, Kye Yong; Lim, In Kyoung; Park, Sang Chul; Lee, Seong Oh; Park, Hyun Sook; Choi, Yang Kyu; Hyun, Byung Hwa
CORPORATE SOURCE: Department of Pathology, Chung-Ang University College of Medicine, Seoul, S. Korea
SOURCE: Carcinogenesis (1999), 20(8), 1541-1548
CODEN: CRNGDP; ISSN: 0143-3334
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The tumor-promoting effect of nodularin during carcinogenesis was investigated. Male Fischer 344 rats were injected with nodularin for 10 wk from week 3 after N-nitrosodiethylamine initiation without partial hepatectomy. Rats were further maintained for 10 wk after the cessation of nodularin and were periodically killed. In contrast to the minimal foci in the DEN and nodularin alone groups, treatment with DEN and nodularin produced four kinds of nodules with eosinophilic, clear, mixed and basophilic cells. After the cessation of nodularin, the maximally increased no., but not the area, of glutathione S-transferase placental form-pos. [GST-P(+)] nodules at week 12 decreased significantly and the appearance of two types of hyperplastic nodules was noted by GST-P **immunostaining**; homogeneously stained dense nodules (DN) and heterogeneously stained pale nodules (PN), which appeared only after the cessation of nodularin. DN were well circumscribed by enzyme-altered cells, as opposed to poorly in PN. Moreover, normal-appearing hepatocytes replaced the enzyme-altered cells in PN. In contrast to the higher PCNA index in GST-P(+) DN, the background level returned to that of the control at week 15. PCNA indexes in DN were significantly higher than in PN, which were still higher than the control, indicating that nodularin affected the PCNA index differentially in the altered and unaltered

hepatocytes. However, nodularin without DEN initiation significantly increased the PCNA index through initial cell death and subsequent hepatocyte proliferation. These results suggest that: (i) nodularin has a promoting effect by inducing hepatocyte proliferation in both enzyme-altered hyperplastic nodules and the surrounding parenchyma; (ii) proliferation is transient in background cells but not in enzyme-altered hepatocytes; (iii) GST-P(+) DN can be regarded as progressive and GST-P(+) PN as regressive, revealed by both **immunohistochem.** and PCNA index.

IT **118399-22-7**, Nodularin
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(effect of nodularin on expression of glutathione transferase placental form and proliferating cell nuclear **antigen** in nitrosodiethylamine initiated hepatocarcinogenesis)

RN 118399-22-7 HCAPLUS

CN Cyclo[L-arginyl-(2S,3S,4E,6E,8S,9S)-3-amino-9-methoxy-2,6,8-trimethyl-10-phenyl-4,6-decadienoyl-D-.gamma.-glutamyl-(2Z)-2-(methylamino)-2-butenoyl-(3S)-3-methyl-D-.beta.-aspartyl] (9CI) (CA INDEX NAME)



REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 28 OF 33 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1999:362567 HCAPLUS
DOCUMENT NUMBER: 131:167565
TITLE: Genetic, morphological, and toxicological variation among globally distributed strains of Nodularia (Cyanobacteria)
AUTHOR(S): Bolch, Christopher J. S.; Orr, Philip T.; Jones, Gary J.; Blackburn, Susan I.
CORPORATE SOURCE: School of Plant Science, University of Tasmania, Hobart, 7001, Australia
SOURCE: Journal of Phycology (1999), 35(2), 339-355
CODEN: JPYLAJ; ISSN: 0022-3646
PUBLISHER: Phycological Society of America
DOCUMENT TYPE: Journal
LANGUAGE: English

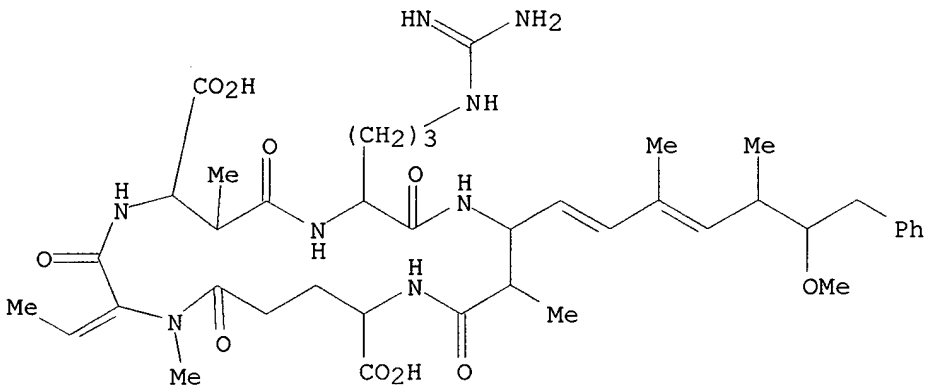
AB Morphol., toxicol., and genetic variation was examd. among 19 strains of Nodularia. The strains examd. could be morphol. discriminated into four groups corresponding to N. spumigena Mertens, N. sphaerocarpa Bornet et

Flahault, and two strains that did not clearly correspond to currently accepted Nodularia species. Genetic variation was examd. using nucleotide sequencing of the phycocyanin intergenic spacer region (cpcBA-**IGS**) and RAPD-PCR. The PCR-RFLP of the cpcBA-**IGS** differentiated four genotypes corresponding to the four morphol. groups. However, nucleotide sequencing of 598 bp of the 690-bp fragment showed that one of the three strains corresponding to N. sphaerocarpa (PCC 7804) was genetically divergent from the other two, suggesting that it constitutes a distinct species. Nucleotide variation within the morphospecies groups was limited (<1%), and all 14 Australian strains of N. spumigena possessed identical cpcBA-**IGS** sequences. The RAPD-PCR differentiated the same groups as the cpcBA sequencing and discriminated each of the seven different Australian populations of N. spumigena. Strains from within a bloom appeared genetically identical; however, strains isolated from different blooms could be sepd. into either a western or a southeastern Australian cluster, with one strain from western Australia showing considerable genetic divergence. The pattern of variation suggests that individual blooms of N. spumigena are clonal but also that Australian N. spumigena populations are genetically distinct from each other. Examn. of genetic distance within and between blooms and within and between morphol. groups showed clear genetic discontinuities that, in combination with the cpcBA-**IGS** data, suggest that Nodularia contains genetically distinct morphospecies rather than a continuous cline of genetic variation. Furthermore, these morphospecies are genetically variable, exhibiting hierarchical patterns of genetic variation on regional and global scales. Prodn. of the hepatotoxin nodularin was not restricted to one genetic lineage but was distributed across three of the five genotypic groups. A strain of N. spumigena from a nontoxic Australian population was found to fall within the range of genetic variation for other toxic Australian strains and appears to be a unique nontoxic strain that might have arisen by loss of toxin prodn. capacity.

IT **118399-22-7**, Nodularin
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(genetic, morphol., and toxicol. variation among globally distributed strains of Nodularia (Cyanobacteria))

RN 118399-22-7 HCAPLUS

CN Cyclo[L-arginyl-(2S,3S,4E,6E,8S,9S)-3-amino-9-methoxy-2,6,8-trimethyl-10-phenyl-4,6-decadienoyl-D-.gamma.-glutamyl-(2Z)-2-(methylamino)-2-butenoyl-(3S)-3-methyl-D-.beta.-aspartyl] (9CI) (CA INDEX NAME)



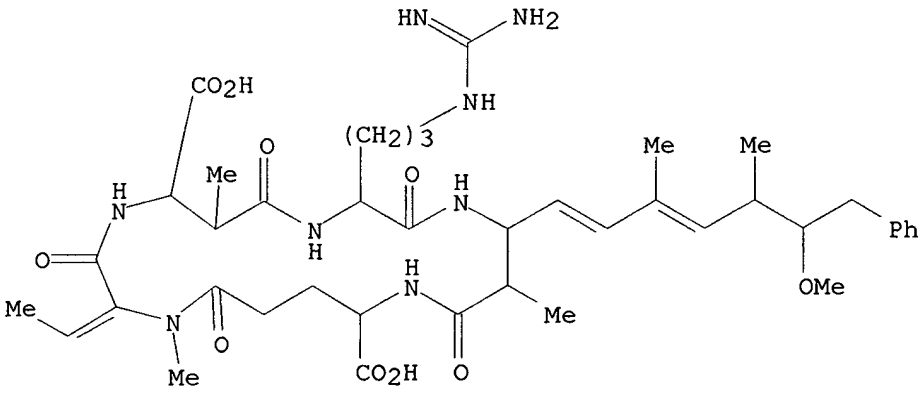
REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 29 OF 33 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:34253 HCAPLUS
DOCUMENT NUMBER: 130:247910
TITLE: Microcystins and nodularins, hepatotoxic cyclic peptides of cyanobacterial origin
AUTHOR(S): Moroder, Luis; Rudolph-Bohner, Sabine
CORPORATE SOURCE: Max-Planck-Institut fur Biochemie, Martinsried, D-82152, Germany
SOURCE: Studies in Natural Products Chemistry (1998), 20(Structure and Chemistry (Part F)), 887-920
CODEN: SNPCE2
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 114 refs. The harmful effects of cyanobacteria (blue-green algae) that grow worldwide in eutrophic fresh and brackish water as well as in marine environments, were originally noted more than a century ago, but only recently was it shown that these organisms produce a variety of bioactive compds. Among these the microcystins are one important group of cyanobacterial toxins that are involved in poisoning of animals and in human health problems around the world. The microcystins are cyclic heptapeptides characterized by a common invariable structure contg. a few variable sections, and all are potent toxins that inhibit the action of type-1 and type-2A protein phosphatases, two of the major serine/threonine specific protein phosphatases in eukaryotic cells, and thus are potent liver tumor promoters. While there is ample information as to the toxicity of these cyanobacterial peptides, their mechanism of action at mol. level as well as their three-dimensional structure in soln. and in the enzyme-bound state have only recently been disclosed. Because of their profound cellular effects, their use as pharmacol. probes for enzyme functions may facilitate the understanding of a large diversity of physiol. processes that are under the control of reversible phosphorylation. Similarly, knowledge of their mode of action may possibly lead to the design of new classes of phosphatase inhibitors as potential anti-tumor agents, anti-inflammatories and **immunosuppressants**.

IT **118399-22-7P**, Nodularin
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); MFM (Metabolic formation); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PREP (Preparation)
(microcystins and nodularins, hepatotoxic cyclic peptides of cyanobacterial origin)

RN 118399-22-7 HCAPLUS
CN Cyclo[L-arginyl-(2S,3S,4E,6E,8S,9S)-3-amino-9-methoxy-2,6,8-trimethyl-10-phenyl-4,6-decadienoyl-D-.gamma.-glutamyl-(2Z)-2-(methylamino)-2-butenoyl-(3S)-3-methyl-D-.beta.-aspartyl] (9CI) (CA INDEX NAME)



REFERENCE COUNT: 143 THERE ARE 143 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 30 OF 33 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1995:624109 HCAPLUS
DOCUMENT NUMBER: 123:109726
TITLE: Novel monoclonal antibodies against microcystin and their protective activity for hepatotoxicity
AUTHOR(S): Nagata, Satoshi; Soutome, Hiroshi; Tsutsumi, Tomoaki; Hasegawa, Akihiro; Sekijima, Masaru; Sugamata, Masao; Harada, Ken-ichi; Suganuma, Masami; Ueno, Yoshio
CORPORATE SOURCE: Faculty Pharmaceutical Sciences, Science University Tokyo, Tokyo, 162, Japan
SOURCE: Natural Toxins (1995), 3(2), 78-86
CODEN: NATOEE; ISSN: 1056-9014
PUBLISHER: Wiley-Liss
DOCUMENT TYPE: Journal
LANGUAGE: English

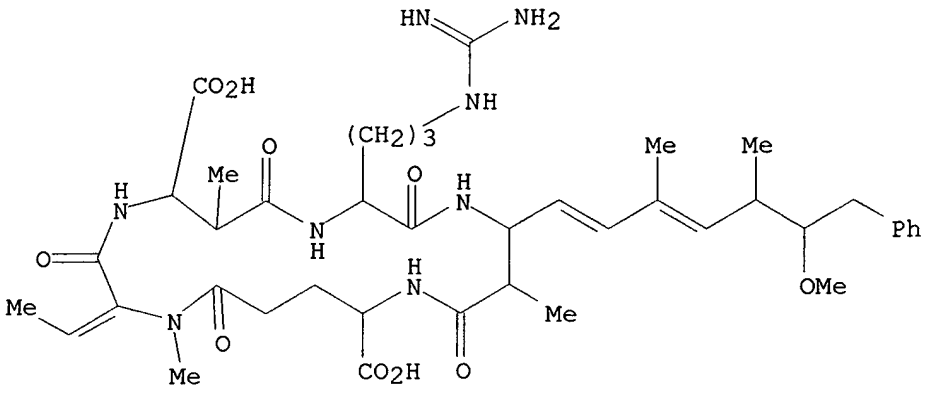
AB Six monoclonal **antibodies** (MAbs) to microcystin-LR(MCLR), a cyclic heptapeptide hepatotoxin isolated from the cyanobacterium Microcystis aeruginosa, were produced. They showed the protective effects on hepatotoxicity of MCLR in vitro and in vivo, and on the inhibition of protein phosphatase by MCLR. Competitive **ELISAs** with various microcystins revealed that the six MAbs recognized a part of the mol., in particular, a tertial structure around Adda, 3-amino-9-methoxy-2,6,8-trimethyl-10-phenyldeca-4,6-dienoic acid. The specificity of these MAbs varied slightly. In primary rat hepatocyte cultures, all MAbs showed protective effects against the MCLR-induced cell damages, assessed by morphol. changes, lactate dehydrogenase release into the medium, and a calorimetric assay to measure the cell viability using a tetrazolium dye. The M8H5 MAb, showing the highest affinity for MCLR, blocked the lethal effects and hepatocellular damage to mice. In addn., M8H5 MAb recovered protein phosphatase 2A inhibition by MCLR in a dose-dependent manner, while phosphatase inhibition by okadaic acid was not affected. Thus, the MAbs specifically reacted with the microcystins and prevented their biol. activities. This is the first report on the protective effects of specific monoclonal **antibodies** on MCLR-induced toxicity.

IT **118399-22-7**, Nodularin
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL

(Biological study); PROC (Process)
(monoclonal **antibodies** to microcystin-LR cross-reactivity with)

RN 118399-22-7 HCAPLUS

CN Cyclo[L-arginyl-(2S,3S,4E,6E,8S,9S)-3-amino-9-methoxy-2,6,8-trimethyl-10-phenyl-4,6-decadienoyl-D-.gamma.-glutamyl-(2Z)-2-(methylamino)-2-butenoyl-(3S)-3-methyl-D-.beta.-aspartyl] (9CI) (CA INDEX NAME)



L12 ANSWER 31 OF 33 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1995:487217 HCAPLUS

DOCUMENT NUMBER: 122:260676

TITLE: **Immuno**-gold localization of hepatotoxins in cyanobacterial cells

AUTHOR(S): shi, Liang; Carmichael, Wayne W.; Miller, Iain

CORPORATE SOURCE: Dep. Biol. Sci., Wright State Univ., Dayton, OH, 45435, USA

SOURCE: Archives of Microbiology (1995), 163(1), 7-15
CODEN: AMICCW; ISSN: 0302-8933

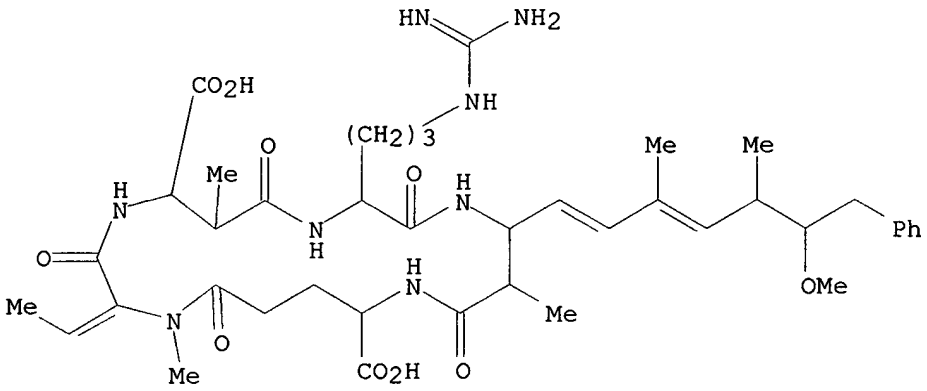
PUBLISHER: Springer

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A polyclonal **antibody** against the potent hepatotoxic cyclic peptide microcystins and nodularins was used in conjunction with **immuno**-gold labeling to localize the toxins in three strains of cyanobacteria. Ultrastructurally, there were no major differences between unicellular Microcystis aeruginosa strain PCC 7820 (toxin-producing strain) and M. aeruginosa strain UTEX 2063 (non-toxin-producing strain), except that M. aeruginosa PCC 7820 cells had a sheath. The thickness of the sheath was about 12 nm and was distinguishable from the cell wall at the ultrastructural level only when the specimen was stained en bloc with uranyl acetate. Microcystins and nodularin were found in M. aeruginosa PCC 7820 and Nodularia spumigena strain L-575 resp., but not in nontoxic M. aeruginosa UTEX 2063. In M. aeruginosa PCC 7820 cells, microcystin was found primarily in the thylakoid area and nucleoid, with smaller amts. in the cell wall and sheath. Only nonspecific labeling was found in other cellular inclusions, such as polyhedral bodies, cyanophycin granules and membrane-limited inclusions. In Nodularia spumigena L-575, nodularin was found in both vegetative cells and heterocysts with a distribution similar to that in M. aeruginosa PCC 7820.

IT **118399-22-7**, Nodularin
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(hepatotoxin subcellular localization in cyanobacteria).
RN 118399-22-7 HCAPLUS
CN Cyclo[L-arginyl-(2S,3S,4E,6E,8S,9S)-3-amino-9-methoxy-2,6,8-trimethyl-10-phenyl-4,6-decadienoyl-D-.gamma.-glutamyl-(2Z)-2-(methylamino)-2-butenoyl-(3S)-3-methyl-D-.beta.-aspartyl] (9CI) (CA INDEX NAME)



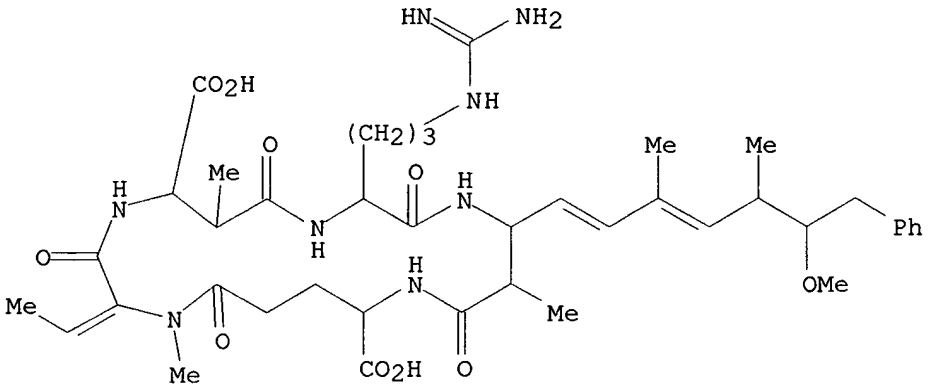
L12 ANSWER 32 OF 33 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1995:302008 HCAPLUS
DOCUMENT NUMBER: 122:98883
TITLE: Use of a colorimetric protein phosphatase inhibition assay and **enzyme linked immunosorbent** assay for the study of microcystins and nodularins
AUTHOR(S): An, JiSi; Carmichael, Wayne W.
CORPORATE SOURCE: Dep. Biological Sciences, Wright State Univ., Dayton, OH, 45435, USA
SOURCE: Toxicon (1994), 32(12), 1495-507
CODEN: TOXIA6; ISSN: 0041-0101
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Using a rabbit anti-microcystin-LR polyclonal **antibody** prepn., the cross-reactivity with 18 microcystin and nodularin variants was tested. A hydrophobic amino acid, 3-amino-9-methoxy-10-phenyl-2,6,8-trimethyl-deca-4(E),6(E)-dienoic acid (Adda), which has the (E) form at the C-6 double bond in both microcystin and nodularin, was found essential for these toxins to express **antibody** specificity. Modification of -COOH in glutamic acid of microcystin and nodularin did not alter their **antigenicity**. **Antibody** cross-reactivity of these toxins was compared with their ability to inhibit protein phosphatase type 1 (PP1). Detection of PP1 inhibition was done by measuring the inhibition effect of the toxins on p-nitrophenol phosphate activity toward PP1. PP1 was obtained as recombinant PP1 expressed in E. coli. The inhibition effect of five microcystins and two nodularins on recombinant PP1 activity toward p-nitrophenol phosphate was measured in a microwell plate reader. The concn. of microcystin-LR causing 50% inhibition of recombinant PP1

activity (IC50) was about 0.3 nM, while that of two modified microcystins had a significantly higher IC50. Microcystin-LR and nodularin with the (z) form of Adda at the C-6 double bond or having the monoester of glutamic acid did not inhibit PP1. These three toxins were also nontoxic in the mouse bioassay. These results show the importance of Adda and glutamic acid in toxicity of these cyclic peptides and that PPI inhibition is related to the toxins' mechanism of action.

IT **159516-66-2**
RL: ANT (Analyte); ANST (Analytical study)
(colorimetric protein phosphatase inhibition assay and **enzyme linked immunosorbent** assay for the study of microcystins and nodularins)

RN 159516-66-2 HCAPLUS

CN Cyclo[(Z)-2,3-didehydro-N-methyl-2-aminobutanoyl-erythro-3-methyl-D-.beta.-aspartyl-L-arginyl-(2S,3S,4E,6Z,8S,9S)-4,5,6,7-tetradehydro-9-methoxy-2,6,8-trimethyl-10-phenyl-3-aminodecanoyl-D-.gamma.-glutamyl] (9CI) (CA INDEX NAME)



L12 ANSWER 33 OF 33 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1989:630287 HCAPLUS
DOCUMENT NUMBER: 111:230287
TITLE: Production and characterization of **antibodies** against microcystins
AUTHOR(S): Chu, Fun S.; Huang, Xuan; Wei, R. D.; Carmichael, W. W.
CORPORATE SOURCE: Food Res. Inst., Univ. Wisconsin, Madison, WI, 53706, USA
SOURCE: Applied and Environmental Microbiology (1989), 55(8), 1928-33
CODEN: AEMIDF; ISSN: 0099-2240
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Antibodies** against a microcystin (MCYST) leucine-arginine variant (MCYST-LR) were demonstrated 4 wk after immunization of rabbits with either MCYST-LR-polylysine- or MCYST-LR-ethylenediamine-modified **bovine serum** albumin. A RIA, a direct competitive **ELISA** and an indirect competitive **ELISA** were developed for characterization of the **antibodies**. Indirect **ELISA** and RIA revealed that MCYST-LR-ethylenediamine-**bovine**

serum albumin was a better **immunogen**. Competitive RIA and direct **ELISA** revealed that the **antibodies** had good cross-reactivities with an MCYST-arginine-arginine variant (MCYST-RR), MCYST-LR, and MCYST-tyrosine-arginine variant (MCYST-YR), and nodularin (NODLN); they had lower reactivities with variants MCYST-leucine-tyrosine (MCYSt-LY) and MCYST-leucine-alanine (MCYST-LA). The **antibodies** did not cross-react with ozonolyzed MCYST-LR. The concns. causing 50% inhibition of binding of reduced MCYST-LR to the **antibodies** by MCYST-RR, MCYST-LR, MCYST-YR, NODLN, MCYST-LA, and MCYST-LY in the RIA were 43, 105, 112, 503, 671, and 1,920 ng/mL, resp. The concns. causing 50% inhibition of binding of MCYSt-LR-horseradish peroxidase to the **antibodies** by MCYST-RR, MCYST-LR, MCYST-YR, NODLN, MCYST-LY, and MCYST-LA in the **ELISA** were 1.75, 2.2, 3.4, 4.6, 50, and 114 ng/mL, resp.

IT **118399-22-7**, Nodularin
RL: BIOL (Biological study)
(**antibodies** to, prepn. and specificity of)

RN 118399-22-7 HCAPLUS

CN Cyclo[L-arginyl-(2S,3S,4E,6E,8S,9S)-3-amino-9-methoxy-2,6,8-trimethyl-10-phenyl-4,6-decadienoyl-D-.gamma.-glutamyl-(2Z)-2-(methylamino)-2-butenoyl-(3S)-3-methyl-D-.beta.-aspartyl] (9CI) (CA INDEX NAME)